

L

L Scale

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Synonyms

Lie scale

Definition

One of the original validity scales on the Minnesota Multiphasic Personality Inventory (MMPI) and its revisions, the L scale consists of 15 items designed to detect attempts to avoid responding honestly. The items reflect patterns of behavior that are socially desirable but only found in the most conscientious individuals. “True” is the non-elevating response for all items, making the scale also sensitive to systematic response bias. There is good face validity to these items; however, because of their transparency, the scale may not detect more sophisticated attempts to respond dishonestly. Elevations on this scale have been associated with denial and lack of psychological sophistication. In addition to its value in the validation of MMPI data, the clinical neuropsychologist may find value in the L scale in validating

information obtained in the clinical interview. Readers are referred to the MMPI entry for a discussion of limitations of this self-report measure when used with neuropsychological populations (see also Gass 2006; Lezak et al. 2004).

Cross-References

- ▶ [F Minus K Index](#)
- ▶ [F Scale](#)
- ▶ [Fake Bad Scale](#)
- ▶ [Faking Good, Bad](#)
- ▶ [K Scale](#)
- ▶ [True Response Inconsistency Scale \(TRIN, MMPI\)](#)
- ▶ [Validity Scales \(MMPI\)](#)
- ▶ [Variable Response Inconsistency Scale \(VRIN, MMPI\)](#)

References and Readings

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L'état Lacunaire

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Synonyms

Lacunar state

Definition

In *L'état lacunaire*, or lacunar state, the brain contains multiple small infarcts or lacunes, usually in the deep structures, especially the basal ganglia.

Current Knowledge

Similar to lacunar strokes, the lacunar state is associated with hypertension and atherosclerosis, the latter being present especially in the small deep vessels in the brain. Many small infarcts can result in dementia, characterized by loss of recent memory, alterations in orientation to time and space, and occasionally paranoia. Lacunar state is a common cause of vascular dementia. There also can be headache, vertigo, and light-headedness. Sensory loss and motor deficits such as ataxia, hemiparesis, and dysarthria, may occur, presenting similarly to lacunar stroke syndromes. Although the diagnosis can be made on clinical grounds, CT scanning and magnetic resonance imaging usually clearly demonstrate the multiple small cerebral infarctions.

Cross-References

- [Cerebrovascular Disease](#)
- [Lacunar Infarction](#)

References and Readings

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La Belle Indifference

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Synonyms

Belle indifference

Definition

La belle indifference is defined in DSM-5 as a “lack of concern about the nature or implications of the symptom” and is listed as an associated feature supporting the diagnosis of conversion disorder (APA 2013, p. 320). Extant neurobiological models converge on the conceptualization of conversion symptoms as involuntary responses to threat reflecting errors in body state information processing and representation (Kozłowska 2005). Theories suggesting frontal lobe hypoactivation as an explanation for apathy and indifference have also been proposed (Spence et al. 2000) as well as theories suggesting a link to right hemispheric dysfunction (Stone et al. 2006).

Cross-References

- [Anosodiaphoria](#)
- [Anosognosia](#)
- [Apathy](#)

References and Readings

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- Kozłowska, K. (2005). Healing the disembodied mind: Contemporary models of conversion disorder. *Harvard Review of Psychiatry*, 13, 1–13.
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- Stone, J., Smyth, R., Carson, A., Warlow, C., & Sharpe, M. (2006). La belle indifference in conversion symptoms and hysteria. *British Journal of Psychiatry*, 188, 204–209.

Lacunar Infarction

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Synonyms

LACI; Lacunar stroke; Lacunar stroke syndrome (LACS); Lacune

Definition

A lacunar infarction is a small (less than 15 mm) deep subcortical area of brain damage, usually resulting from occlusion of the tiny (200–800 μ) deep penetrating lenticulostriate arteries that normally provide blood supply to the deeper subcortical brain tissues, such as the basal ganglia, internal capsule, thalamus, and brain stem.

Current Knowledge

It is thought that prolonged exposure to hypertension, diabetes, smoking, and other factors induces

the processes of lipohyalinosis (*small vessel disease of the brain*) and microatheroma (*tiny accumulations and swelling of artery walls that are comprised of cell debris, lipids, calcium, and fibrous tissue*) in the small blood vessels that feed the subcortical areas, ultimately causing their occlusion. It is estimated that lacunar infarcts account for 25% of all ischemic strokes, with an incidence of approximately 15 per 100,000 per year. They are more frequent in men and in African Americans, Hispanics, and Asians.

There are five clinical stroke syndromes associated with lacunar infarctions, each with a distinct presentation. *Pure motor hemiplegia* is most common, causing about one-third to one-half of all lacunar strokes. It involves only complete or partial paralysis of the arm, leg, and/or face. *Ataxic hemiparesis* is associated with a combination of cerebellar and motor symptoms, including weakness and clumsiness, on the ipsilateral side of the body, affecting the leg more than the arm; it is also called hemiataxia - hemiparesis. *Dysarthria-clumsy hand syndrome* is associated with weakness of the hand and facial muscles. In *pure sensory stroke*, the patient has a transient or persistent contralateral numbness or dysesthetic pain. *Mixed sensorimotor stroke* causes hemiparesis and ipsilateral sensory loss.

Lacunar strokes can be treated with thrombolysis if diagnosed sufficiently early. Alternatively, antiplatelet therapy or anticoagulation can be used. Outcome is generally good, with mortality less than 5%, and complete recovery of independent function in up to 80% at 1 year.

Cross-References

- ▶ [Anticoagulation](#)
- ▶ [Antiplatelet Therapy](#)
- ▶ [Atherosclerosis](#)
- ▶ [Cerebrovascular Disease](#)
- ▶ [Ischemic Stroke](#)
- ▶ [Pure Motor Stroke](#)

- Small Vessel Ischemic Disease
- Thrombolysis

References and Readings

- Baumgartner, R. W., Sidler, C., Mosso, M., & Georgiadis, D. (2003). Ischemic lacunar stroke in patients with and without potential mechanism other than small-artery disease. *Stroke*, 34, 653–659.
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Lamotrigine

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Generic Name

Lamotrigine

Brand Name

Lamictal, Labileno, and Lamictin

Class

Anticonvulsant, mood stabilizer

Proposed Mechanism(s) of Action

Blocks voltage-sensitive sodium channels and inhibits glutamate release.

Indication

Bipolar I disorder (maintenance), partial seizures, and seizures associated with Lennox-Gastaut syndrome.

Off-Label Use

Bipolar depression, bipolar mania, schizophrenia (psychosis), neuropathic pain, and chronic pain.

Side Effects

Dizziness, diplopia, headache, ataxia, blurred vision, rhinitis, somnolence, insomnia, and fatigue.

Serious

Stevens-Johnson rash, organ failure, epidermal necrolysis, drug hypersensitivity, and sudden unexplained death in epileptic patients.

Common

Skin rash, ataxia, headache, tremor, fatigue, sedation, nausea, vomiting, constipation, flu syndrome, pharyngitis, and asthenia.

References and Readings

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- Stahl, S. M. (2007). *Essential psychopharmacology: The prescriber's guide* (2nd ed.). New York: Cambridge University Press.

Additional Information

Drug Interaction Effects: http://www.drugs.com/drug_interactions.html.

Drug Molecule Images: <http://www.worldofmolecules.com/drugs/>.

Free Drug Online and PDA Software: www.epocrates.com.

Gene-Based Estimate of Drug interactions: <http://mhcd.daytondcs.com:8080/cgi-bin/ddiD4?ver=4&task=getDrugList>.

Pill Identification: http://www.drugs.com/pill_identification.html.

Landau-Kleffner Syndrome

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Synonyms

Acquired epileptic aphasia

Definition

Landau-Kleffner Syndrome (LKS) is an epileptic encephalopathy that is marked by sudden and relatively rapid onset of aphasia in a child with normal or near normal language development. The acquired aphasia classically begins with a verbal auditory agnosia (VAA), or word deafness, and often progresses to expressive language impairment. Sleep-activated epileptiform abnormalities maximally over the temporal regions are a defining feature. Clinical seizures are evident in most cases, but they are not necessary for the diagnosis.

Epidemiology

LKS is considered to be an especially rare epilepsy syndrome, constituting about 0.2% of childhood epilepsy syndromes. Its prevalence, however, has increased in recent years likely due to better awareness. LKS is believed to be almost twice as common in males.

A genetic predisposition for LKS has not been identified. Rather, some have suggested that an underlying autoimmune condition may be responsible for at least a subset of cases. The cognitive

changes associated with LKS reflect an epileptic encephalopathy, which refers to a loss of cortical function in association with epileptiform abnormalities. These abnormalities are believed to create cerebral dysrhythmia with abnormal neuronal network synchronization, resulting in cognitive dysfunction that can fluctuate in concert with the severity of the EEG. Original reports of LKS suggested language functioning resolved with normalization of the EEG, but more recent reports clearly demonstrate functional impairments that may not resolve. While this likely reflects structural cortical changes, imaging studies are typically normal in patients with LKS. The majority of cases are believed to be idiopathic, but recent classification refers to the etiology as unknown. Symptomatic cases of LKS have been described.

Natural History, Prognostic Factors, Outcomes

The typical age of onset for LKS is between the ages of 3 and 7 years, with some criteria suggesting a typical range up to 10 years. About 70% of cases present with sudden language impairment prior to the age of 6 years. LKS typically first presents as verbal auditory agnosia (word deafness) that is characterized by progressive problems with speech comprehension in the presence of normal hearing. Some children with LKS also exhibit an inability to respond to non-speech sounds, such as environmental stimuli (e.g., doorbell, knock on the door, telephone, etc.). The loss of auditory response is precipitous, often occurring over a matter of days, and it can be easily mistaken for hearing impairment. Differential diagnosis of peripheral hearing loss is important. While impairment in receptive language is the defining feature of LKS, subsequent impairment in expressive language is common and tends to reflect a lack of phonological aspects of speech.

Functional outcome in LKS is variable. Despite the good response of clinical seizures and EEG abnormalities to medication intervention, 75–86% of patients may experience residual

language problems of varying severity, and auditory working memory seems to be most sensitive to long-term dysfunction. Later age of onset appears to be correlated with better functional outcomes (after 6 years of age).

The majority of patients with LKS experience clinical seizures (about 70%), but they are typically infrequent and often disappear prior to the age of 15 years. Seizures usually begin around the onset of language impairment, and only about 20% of patients experience seizures beyond the age of 10 years. Partial motor, atypical absence, and generalized tonic-clonic seizures are most common, with about 80% of children exhibiting convulsive seizures. Prognosis does not appear to be affected by seizure frequency or type.

Neuropsychology and Psychology of LKS

All children with LKS should undergo a comprehensive neuropsychological assessment to track developmental changes during the course of the condition. This can help with differential diagnosis and treatment planning. Because children with LKS typically do not exhibit further regression in language functioning after normalization of their EEG, monitoring of cognitive functioning can help track the presence of continued epileptiform abnormalities and potentially maximize functional outcome by helping to inform the need for treatment modifications.

Traditional descriptions of children with LKS suggest that they have no previous history of language dysfunction, but more recent research indicates that 65–75% of children with LKS may have preexisting language problems. The core cognitive deficit in LKS appears to reflect an interference in decoding of phonological aspects of auditory stimuli, which most commonly affects language comprehension but may also interfere with one's ability to identify nonspeech sounds. In their investigation of receptive language impairment in LKS, Korkman et al. (1998) concluded that children with LKS demonstrate selectivity in their auditory processing impairment.

Specifically, children with LKS have specific problems discriminating phonological stimuli, with relative preservation in their ability to discriminate environmental stimuli. This suggests a specific impairment in their ability to decode speech-related auditory stimuli.

Most children with LKS would be expected to exhibit impairment in both receptive and expressive language upon first presentation to a neuropsychologist. Thorough consideration of various aspects of auditory processing should be emphasized, including auditory discrimination and recognition of verbal and nonverbal auditory stimuli. While VAA is the defining language problem in LKS, various types of language problems can be exhibited, including auditory agnosia, verbal agnosia, and an auditory discrimination deficit (Cockerell et al. 2011). Aphasia may fluctuate during the course of LKS, presumably in association with neurological stability in relation to the severity of epileptiform abnormalities. Preferential problems with verbal memory would be expected to go along with the language comprehension problems, though, as discussed previously, functional reorganization may reflect relative preservation of verbal memory later in the course of the condition.

When assessed nonverbally, intellectual ability is traditionally average in LKS, with only a handful of reports suggesting a higher than expected rate of below average performance. VIQ/PIQ discrepancies are inconsistent and, when reported by Mantovani and Landau in 1980, only occurred in the correct direction 50% of the time. However, when it occurred, the difference was significant (ranging from 29 to 55 points).

In studying visual-spatial processing and visual memory in LKS, Mantovani and Landau (1980) found that children with the best language outcomes tended to have poorer performance on the Revised Benton Visual Retention Test (RBVRT). They suggested that this could reflect functional reorganization. Additional studies have also demonstrated impairments in visual-spatial processing and other nonlinguistic cognitive abilities in LKS (42–50%).

Behavioral disturbance in LKS is common, and it often precedes onset, but it is not considered a primary feature of the condition. The rate of behavioral problems ranges as high as 50–66% and tends to be most prominent in children with frontal involvement on EEG (especially hyperactivity). Sleep disruption may contribute to these problems. Autism Spectrum Disorder (ASD) is an important differential in LKS and, given the common history of language regression, can sometimes be difficult to delineate. Later age of onset in LKS is a typical distinguishing feature, though this may be less helpful with recent changes in the diagnostic criteria for ASD. In most cases, children with LKS do not demonstrate restricted, repetitive patterns of behavior, and their social impairments are qualitatively different than ASD. In LKS, children are more likely to demonstrate social problems as a reaction to their deteriorating communication skills from their language regression. This is manifested as social withdrawal and would be expected to be more closely associated with frustration about their inability to communicate effectively.

Evaluation

LKS is distinguished by its characteristic clinical course and features. It can be difficult to make a clinical distinction between LKS and continuous spikes and waves during slow-wave sleep (CSWS), which is associated with more global neuropsychological deterioration. Progressive deterioration of language functioning, especially receptive language, distinguishes LKS from CSWS. The EEG abnormalities in LKS are also more focal than in CSWS.

The EEG in LKS typically reveals multifocal spikes and spike and slow-wave activity most often involving the temporal or posterior regions. The discharges significantly increase during NREM sleep. EEG abnormalities are typically bilateral, but there are reports of cases with only unilateral discharges.

LKS variants have been described to account for clinical presentations that include sleep-activated epileptiform abnormalities without the traditional features of LKS, particularly the classic acquired verbal auditory agnosia. Variants of LKS have been proposed to describe children with regression of more anterior language abilities (anterior LKS), often manifesting as oral-motor apraxia. Children with preexisting language impairment who may or may not exhibit language regression are sometimes described as developmental LKS.

Treatment

As part of treatment planning, all children with LKS should undergo a comprehensive neuropsychological assessment. This can help in clarifying the diagnosis, monitoring the effectiveness of treatment, and planning appropriate educational and therapeutic services. Intensive speech-language therapy is of critical importance for children with LKS. Participation in speech-language therapy should be maximized to allow for the best potential functional outcomes.

Because learning can be variable in LKS, school services should be designed based upon the needs of each individual patient. In general, however, efforts to circumvent deficits in auditory processing are typically helpful. This includes the use of visual mediation during learning and the application of alternative means of communication (e.g., sign language, picture-based communication systems, etc.). Academic services can be enhanced with the assignment of a one-on-one aide, particularly when attention and concentration are also impaired.

Evidence-based recommendations for treating LKS are not available. There are multiple clinical trials being developed that use various combinations of antiepileptic drugs and/or corticosteroids. Corticosteroids or benzodiazepines are recommended as first-line treatments, with some only recommending steroid treatment if benzodiazepines do not work within 3 months. Early and long-term treatments are recommended; however, ongoing language dysfunction following

normalization of the EEG is common. Treatment with antiepileptic drugs (AEDs) in LKS is traditionally believed to be effective for managing seizures, but the benefits for language development are minimal. Valproic acid and clobazam are frequently used, along with ethosuximide and high-dose diazepam. Effectiveness of the ketogenic diet has been demonstrated in some patients with LKS, and multiple subpial transection (MST) has been found to be of benefit in some patients who fail to respond to medication intervention.

Landau-Kleffner syndrome	
EEG signature	Multifocal spike and slow-wave activity most often involving the temporal or posterior region Discharges increase significantly during sleep
Age of onset	3–7 years
Clinical features	Clinical manifestation: loss of language skills, a verbal auditory agnosia often with varying degrees of behavioral and neurocognitive difficulties Semiology: nocturnal focal seizures are more prevalent than tonic and GTCs MRI is typically normal
AED management	Valproic acid, clobazam, ethosuximide, high-dose diazepam Corticosteroids, ACTH, and IVIG are potential treatments with varying degrees of success
Response to treatment with AEDs	Good, but may require corticosteroids
Seizure freedom	Good
Functional outcome	Variable. Outcomes are better with later onset (>3 years) and successful and rapid management of EEG abnormalities

Cross-References

- ▶ [Adrenocorticotrophic Hormone](#)
- ▶ [Aphasia](#)
- ▶ [Auditory Agnosia](#)
- ▶ [Benton Visual Retention Test](#)
- ▶ [Diazepam](#)

- ▶ [Electroencephalography](#)
- ▶ [Encephalopathy](#)
- ▶ [Language](#)
- ▶ [Leiter International Performance Scale, Third Edition](#)
- ▶ [Rolandic Epilepsy](#)
- ▶ [Valproate](#)

Further Reading

Cockerell, I., Bølling, G., & Nakken, K. O. (2011). Landau-Kleffner syndrome in Norway: Long-term prognosis and experiences with the health services and educational systems. *Epilepsy & Behavior*, 21(2), 153–159.

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Van Slyke, P. A. (2002). Classroom instruction for children with Landau-Kleffner Syndrome. *Child Language Teaching and Therapy*, 18, 23–42.

Language

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Definition

One avenue for the communication of thoughts, feelings, and/or ideas, language is comprised of symbols (i.e., vocabulary/words), which are socially agreed upon by members of a given

community/culture (e.g., American-English, French, Spanish, etc.), and includes various regional dialects within those communities/cultures. Language requires the rule-governed use of these symbols (e.g., use of grammar, putting words together to form complete sentences, etc.) and typically includes four domains: (1) verbal expression (e.g., speaking aloud), (2) written expression (e.g., composing a letter, an e-mail, or an essay, etc.), (3) auditory comprehension (e.g., the understanding what others say aloud), and (4) reading comprehension (e.g., the understanding of written text). In the deaf culture, however, various (unspoken) sign languages may be used in lieu of spoken language (e.g., American Sign Language, language does not include the motoric act of moving the articulators (e.g., the lips, tongue, cheeks, vocal folds, etc.)) to pronounce the words (i.e., speech) or the motoric act of constructing the letters with a writing instrument.

Language disorders may result as a part of the sequelae of various developmental disorders (e.g., Down's syndrome or language learning delay), or they may occur following acquired injuries to the brain (e.g., stroke, traumatic brain injury, etc.)

See Also

- [Aphasia](#)
- [Articulation](#)
- [Grammar](#)
- [Speech](#)
- [Writing](#)

Further Reading

- Brown, C. M., & Hagoort, P. H. (Eds.). (2000). *The neurocognition of language*. Oxford: Oxford University Press.
- Owens, R. E. (2014). *Language development: An introduction* (8th ed.). Edinburgh Gate: Pearson Education Limited.
- Papathanasiou, I., Coppens, P., & Potagas, C. (Eds.). (2013). *Aphasia and related neurogenic communication disorders*. Burlington: Jones & Bartlett Learning.

Lashley, Karl Spencer (1890–1958)

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Major Appointments

- 1910–1911 Teaching Fellow, University of Pittsburgh, Pittsburgh, PA, USA
- 1917–1918 Instructor of Psychology, University of Minnesota, Minneapolis, MN, USA
- 1920–1926 Full Professor, University of Minnesota, Minneapolis, MN, USA
- 1926–1929 Research Psychologist, Behavioral Research Fund, Institute for Juvenile Research, Chicago, IL, USA
- 1929–1935 Professor of Psychology, University of Chicago, Chicago, IL, USA
- 1929 President of the American Psychological Association
- 1935–1937 Professor of Psychology at Harvard, Cambridge, MA, USA
- 1937 President of the Eastern Psychological Association
- 1937–1955 Research Professor of Neuropsychology at Harvard, Cambridge, MA, USA
- 1947 President of the American Society of Naturalists
- 1942–1955 Director at the Yerkes Laboratories of Primate Biology, Orange Park, Florida, USA

Major Honors and Awards

- 1927–1930 Lashley served on the National Research Council.
- 1937 Howard Crosby Warren Medal by the Society of Experimental Psychologists.
- 1943 Daniel Giraud Medal for Zoology by the National Academy of Sciences.

- 1951 Named Foreign Member of the Royal Society.
- 1953 William Baly Medal for Physiology by the Royal College of Physicians.
- 1953 LL.D. honorary degree from Johns Hopkins University.

Professional Memberships

American Society of Zoologists, American Physiological Society, Society of Experimental Psychologists, American Society of Human Genetics, American Philosophical Society, American Academy of Arts and Sciences, New York Academy of Sciences (Honorary Member), Florida Psychological Association, National Academy of Science, British Institute for the Study of Animal Behaviour (Honorary Member), American Neurological Association, Harvey Society (Honorary Member), British Psychological Association (Honorary Fellow), Foreign Member of the Royal Society.

Landmark Clinical, Scientific, and Professional Contributions

- Perhaps Lashley's primary contribution to the field of neuropsychology was the manner in which he methodologically examined brain-behavior relations. To this end, he supported the equipotentiality of cortical tissue, a theory initially posited by Pierre Florens, which claimed that behaviors (or cognitive abilities) are dependent on the brain functioning as a whole. This theory also claims that the amount of neural tissue damaged is more important than its location because the remaining cerebral tissue has the potential to take over the functions of the lesioned area(s). This former notion became known as the principle of mass action, which states that the severity of the behavioral deficit is directly proportional to the mass of the lesioned tissue. However, Lashley believed that sensory and motor abilities were, to some extent, "localized" within the cortex.
- In 1929, Lashley published *Brain Mechanisms and Intelligence: A Quantitative Study of Injuries to the Brain*, work that introduced the concepts of mass action and equipotentiality. Using rats, his research examined the effects of cerebral lesions on acquisition and retention of information. This work used a variety of tasks including mazes of varying difficulty, brightness discriminations, and inclined-plane problems (which requires discrimination of the direction of slope of a surface). The major finding was that maze learning performance was negatively affected by brain damage, but this effect depended on the extent of the damage rather than the location. Since the location of the cerebral lesion did not dramatically affect performance, he concluded that "intellect" was not localized in any single region of the brain. This distinction did not necessarily hold true for simpler behaviors. For example, large occipital lesions caused deficits in the brightness discrimination task, but the animals rapidly relearned these discriminations at the same rate as they had initially. He addressed this discrepancy by suggesting that more complex tasks such as the maze learning requires more cortical tissue than the simpler brightness discrimination or inclined-plane tasks.
- Lashley's address as president of the American Psychological Association, entitled "Basic Neural Mechanisms in Behavior," was given to the International Congress of Psychology at Yale University and published in 1930. He discussed two theories of brain functioning: that of localization and reflex theory. Both of these theories propose the specialization of specific brain regions (localization) or single cells (reflex theory) for specific and limited functions. Lashley refuted both hypotheses and proposed that, rather than focusing on where psychological functions are localized, psychologists should address the means through which complex systems are able to exert an influence on each other.
- Lashley's 1938 presidential address to the Eastern Psychological Association ("The

Experimental Analysis of Instinctive Behaviour”) was regarded by some as one of his greatest contributions to comparative psychology. He reasoned that determinants of behavior can be instinctual as well as learned. For example, animal behaviors such as the honey dance of bees, kin recognition, and reproduction activity can all be considered instinctive. He suggested that, at a neural level, all instincts are the result of an activation of specific sensorimotor mechanisms. In his subsequent research, he claimed that just as genetic determinants can be used to describe differences between species, similar determinants can be used to describe differences within species. He also proposed that individual variation within the brain was the cause of variable mental capacity and behavior. For this reason, he opposed attempts at developing standardized cortical maps, including those of Brodmann. In his 1949 presidential address to the American Society of Naturalists, Lashley emphasized the role of materialism, behaviorism, and genetics as determinants of behavior and suggested that, from an evolutionary standpoint, increased capacity and abilities are primary factors that differentiate animals.

Short Biography

Karl Spencer Lashley, the only son of Charles Gilpin Lashley and Margaret Blanche Spencer, was born on June 7, 1890, in Davis, West Virginia. Starting when Lashley was 4, the family began a series of moves that included stays in California, Seattle, and finally Alaska during the 1898 gold rush, before they finally returned to West Virginia in 1899. Despite the lack of regular and formal schooling, Lashley graduated from Davis High School when he was 14 years old, during which time he developed his interest in the natural behavior of animals and steadfast love of nature.

In 1905, Lashley matriculated to the University of West Virginia, where he enrolled in a zoology course taught by neurologist John Black Johnston.

This course had a profound effect on Lashley and not only helped determine his major course of study but formed a basis for his career in the life sciences. From 1906 to 1909, Lashley was a research assistant to Albert M. Reese and worked with the Golgi series of frog brains. He graduated from the University of West Virginia with an A.B. degree in 1910 and was subsequently awarded a teaching fellowship in biology at the University of Pittsburgh. The following year, he completed his thesis on the bacteriology of rotten eggs and earned his Master of Science from the University of Pittsburgh.

Lashley spent the summer of 1911 at Cold Spring Harbor Biological Laboratory on Long Island conducting genetics research on *Stylonychia*, a member of the ciliate family. The following fall, Lashley enrolled in a Ph.D. program in zoology at Johns Hopkins University. After completing his Ph.D. in 1914, Lashley remained at Hopkins as a Bruce Fellow in zoology, conducting field experiments on the behavior of seabirds with John B. Watson. In the fall of 1917, he accepted his first teaching position as instructor of psychology at the University of Minnesota but took a leave of absence after his first year in order to work alongside John B. Watson at the US Interdepartmental Hygiene Board in Baltimore, educating the public about the dangers of venereal disease. In 1920, he returned to the University of Minnesota, where he became a full professor in psychology. In 1926, he moved to Chicago, accepting a position as a research psychologist with the Behaviour Research Fund at the Institute for Juvenile Research. In 1929, he was elected president of the American Psychological Association and also became Professor of Psychology at the University of Chicago, where he remained until 1935.

Between the years 1920 and 1929, Lashley continued to research the functions of the central nervous system, with specific focus on sensory discrimination and the formation and retention of habits in animals. His contributions to the mechanisms of learning during this time were particularly noteworthy. In 1935, he became Professor of

Psychology at Harvard, which involved more administrative work than he preferred, and in 1937 after threatening to resign, he was appointed Research Professor of Neuropsychology, which gave him freedom to pursue research outside Harvard. In 1942, he accepted the Directorship position at the Yerkes Laboratories of Primate Biology in Orange Park, Florida. He retired from this position in 1955, as he dealt with a series of prolonged and difficult medical treatments for hemolytic anemia. After traveling to England to sign the Charter Book of Royal Society, he unexpectedly died in France on August 7, 1958 at the age of 68.

Cross-References

- [Equipotentiality](#)
- [Localization](#)

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Late Effects of Radiation Therapy

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Definition

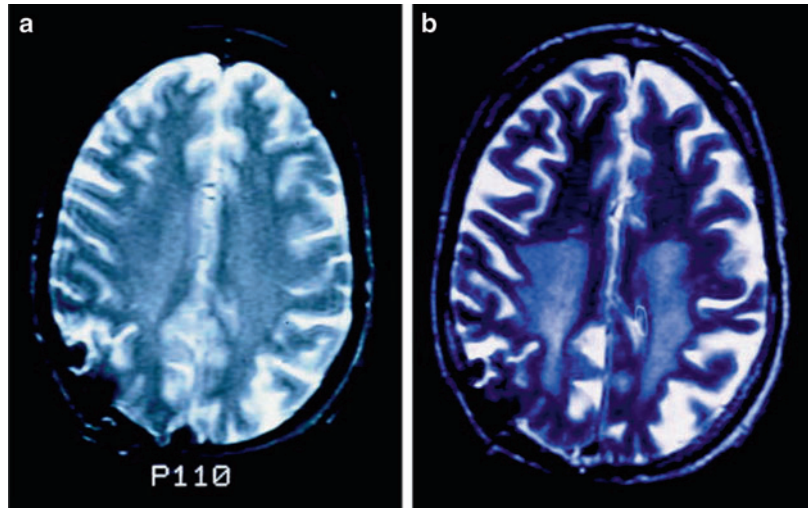
Radiation therapy is considered a necessary treatment for many types of tumor and is frequently used in the CNS for the treatment of primary brain tumors, arteriovenous malformations, small-cell lung cancer, high-risk leukemia, brain metastases, and other neoplasms. However, there are severe iatrogenic late effects of radiotherapy (XRT), which are very significant when they occur in the context of either partial brain fields or whole brain field. Late effects are defined as those occurring after the complete dose of XRT has been administered. XRT is used as an adjunct to surgical resection of the mass, which provides the best cure or prevention of recurrence. The curative effects are not always the goal, and it is also used as prophylaxis, and as palliation, that is, to prolong life expectancy.

Current Knowledge

Neurological effects The late effects of XRT include risks of leukoencephalopathy, radiation necrosis (which is a rare but progressive mass lesion), and functional impairment. Figure 1a, b of the late effects of radiotherapy within the radiation portals of a 43-year-old woman treated for a right parietal glioma at 6 months posttreatment (early-delayed phase), and at 8 years posttreatment (late-delayed phase). There are also neurological effects when critical brain structures are unavoidably included in the radiation fields, such as vasculitis or stroke that can occur when the circle of Willis is involved, blindness when the optic tracts and chiasm are involved, and

Late Effects of Radiation Therapy, Fig. 1

(a) Adult with resected right parietal glioma, with focal field photon radiotherapy to the tumor region, 6 months post completion of radiotherapy. The effects on bilateral posterior parietal lobe are visible in the white matter. (b) Same adult with resected right parietal glioma, without tumor recurrence, 8 years after radiotherapy, with portal fields still visible in the posterior brain



ototoxicity when the auditory canals are involved. Today, every effort is made to avoid these structures. Late effects often injure multiple systems, including but not limited to widespread endocrine system dysfunction, diabetes type 2, chronic renal insufficiency, asthma, cardiac enlargement, and bilateral cataracts.

Cognitive effects The most severe late effects of XRT have become less frequent with improvements in treatment regimens; however, patients remain at very high risk for neurocognitive effects. The late cognitive effects depend on a number of factors, including the area treated, dose burden, patient age, and the time posttreatment (Armstrong et al. 2004). Late effects are not a matter initially of widespread cognitive dementia but are specific and related to the underlying neurophysiological mechanisms (see “► [Early-Delayed Effects of Radiation](#)” and “► [Late-Delayed Effects of Radiation Therapy](#)”). The most well-documented clinical risks for injury that must be differentiated from radiation effects are those of cancer type, radiation regimen, concurrent chemotherapy, and age (Vigliani et al. 1997). However, the risk of eventually developing dementia or mental retardation from large dose burden to the brain may occur, though is not usually seen until many years, if not decades, later.

The new technique of proton therapy is being used to reduce the dose to normal-appearing brain

by 50–75%, which is hoped to reduce the late cognitive, sensory, and endocrine neurotoxicities. Disease control with proton is as good or better as that achieved with standard photon radiotherapy (MacDonald et al. 2011). Early conference reports indicate similar cognitive outcomes, but there are no reports yet that conclusively compare the techniques.

Cross-References

- [Early-Delayed Effects of Radiation](#)
- [Late-Delayed Effects of Radiation Therapy](#)
- [Radiation Injury](#)

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Late Life Function and Disability Index

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Synonyms

LL-FDI

Description

The Late Life Function and Disability Index (LL-FDI) was designed in 1992 to assess and demonstrate change over time or after an intervention for older adults in two outcome domains: disability and function (Haley et al. 2002; Jette et al. 2002). The disability component contains 16 items in two dimensions: frequency of performance and limitation in performance of life tasks. Each dimension contains two disability domains; within frequency, there are personal and social role domains, and within limitation there are instrumental and management role domains (Jette et al. 2002). The function component contains 32 items in three dimensions: upper extremity, basic lower extremity, and advance lower extremity functions. The three dimensions did not subdivide into different domains. Raw scores are transformed based on a Rasch model to scaled scores ranging from 0 to 100 with higher scores corresponding to better levels of functioning.

Historical Background

The LL-FDI is based upon Nagi's disablement framework for assessing functional limitations and disability components (Nagi 1991) as well

as the World Health Organization's International Classification of Functioning, Disability, and Health (ICF) (WHO 2001). Functional limitations are conceptualized as limitations of the ability to perform actions or activities. Disability comprises performance of expected life tasks within a typical sociocultural and physical environment.

Psychometric Data

Scaling: The frequency and limitation dimensions of the LL-FDI disability component exhibited good item separation along a hierarchy from easy to difficult items to endorse; this is supportive of a scale with good scaling (Jette et al. 2002). Similar findings were noted for the function component (Jette et al. 2002).

Reliability: With an average interval of 12 days, test-retest intraclass correlations ranged between 0.68 and 0.82 for the disability component and between 0.91 and 0.98 for the functional limitation component (Haley et al. 2002; Jette et al. 2002).

Validity: In the original articles describing the development of the LL-FDI, the sample was divided into 4 groups: severe, moderate, slight, and no functional limitations based upon scores on the physical function scale of the SF-36. Both the functional limitation and disability components discriminated between the 4 groups (Haley et al. 2002; Jette et al. 2002). In a comparison of the LL-FDI and scores on a short physical performance battery (SPPB) and a self-paced walk test, correlations between the two lower extremity functional limitation components and the SPPB and walk test were significantly stronger than with the upper extremity functional limitation component (Sayers et al. 2004). In a comparison between the LL-FDI and the physical functioning scale of the SF-36 and the London Handicap Scale, the LL-FDI demonstrated less ceiling effects and better precision across the range of function and disability (Dubuc et al. 2004).

Clinical Uses

The LL-FDI, and its subscales, has demonstrated sensitivity to change in a number of studies. Most scales showed small-to-moderate effect sizes in studies that demonstrated response to treatment/intervention. There is not enough evidence currently to define a clinically meaningful difference on the LL-FDI or its subscales. For a complete review, please see Beauchamp et al. (2014).

Cross-References

- [Disability](#)
- [Functional Status](#)
- [SF-36/SF-12](#)

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Late-Delayed Effects of Radiation Therapy

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Synonyms

Late effects

Definition

The late-delayed radiation symptoms are most commonly seen in the neurological, neurocognitive, and endocrine systems. Late-delayed radiation effects on the central nervous (CNS) system are iatrogenic injuries that are irreversible and possibly progressive. Neural substrates include vasculopathies and capillary damage, stroke, demyelination, disruption of cellular mitosis, radiation necrosis, diaschisis, destruction of the hypothalamic–pituitary axis, and gliosis. Late-delayed effects often present as leukoencephalopathy within the tumor field; this gross change is more commonly seen on MRI or CT at higher total radiation doses.

Historical Background

Changes have been retrospectively described several months to many years posttreatment (for review, see Armstrong et al. 2004; Crossen et al. 1994; DeAngelis et al. 1989). Declines have been reported using PET and [¹¹C] methionine, an amino acid marker, in gray matter remote from the tumor during several months to over 1 year after irradiation (Sato et al. 1995; Shishido et al. 1990). Neural disruption can also occur; in a case study, a patient with a low-grade mixed glioma showed a gradual decrease following RT in amino

acid metabolism in the gray matter contralateral to the tumor (Sato et al. 1995), whereas both CT and MR were unrevealing. The temporal pattern of the onset of late-delayed symptoms is uncertain and likely influenced by other factors. Onset of clinically apparent symptoms has been reported as early as 2 years posttreatment, and as late as 10–20 years posttreatment, often attributed to degeneration of vascular tissue. There are few prospective studies of the late-delayed time points in patients with non-malignant disease. Results in patients with lymphoma, leukemia, small-cell lung cancer, and other malignant histologies have demonstrated that groups of patients with malignant cancer are often neuropsychologically impaired at baseline even when there are no CNS tumors. Because radiation is most often given to higher-grade neoplasms, cognitive decline may also be associated with disease progression versus radiation effects (Archibald et al. 1994; Armstrong et al. 2005).

Current Knowledge

Cognitive effects in adults: While retrospective reports and individual case studies demonstrate the severity that late-delayed damage from RT can cause, there are few prospective studies on the actual frequency of such severe damage in both children and adults. Vigliani and colleagues' prospective study provided outcome at 4 years (Vigliani et al. 1996). One patient demonstrated a decline in cognitive function, two patients improved, and one patient was unchanged. Armstrong and colleagues' prospective longitudinal study of 26 adult patients with low-grade, supratentorial, brain tumors extending 6 years from treatment found selective cognitive decline emerging only at the 5-year endpoint, limited to visual memory, in half of the patients who were treated with moderately high, part field radiation (mean of 5,400 cGy, fractions of 180 cGy). Ratings of clinical MRIs (T2-weighted and FLAIR images) showed, also in half of the patients, mild accumulation of hyperintensities with onset from 6 months to 3 years and with no further

progression to 6 years. White matter atrophy and total hyperintensities demonstrated the effect, and subcortical and deep white matter, corpus callosum, cerebellar structures, and pons accounted for these changes over time. Klein and colleagues reported that radiation-related memory impairment in their adult patients with low-grade tumors only occurred for those receiving dose fractions that exceeded 200 cGy (Klein et al. 2002). Early-delayed radiation effects are not predictive of late-delayed effects (Armstrong et al. 2000), and those who develop somnolence during the acute phase of radiotherapy acquire no extra risk for late-delayed neuropsychological deficits (Berg et al. 1983).

Cognitive effects in children: A consensus has been reached from overwhelming evidence that RT compromises the developing brain and that younger children have worse outcomes than older children (Armstrong et al. 2004; Mulhern et al. 1992). Younger children may be more vulnerable to decline prior to RT due to the interaction of their tumor and treatment with their brain development, which is thought to be due to the iatrogenic effects on their more actively myelinating brain regions, though developmental effects from injury to hippocampal neuroblast progenitors and immune-mediated processes are also implicated.

Radcliffe and colleagues reported on prospective findings in children treated with radiation therapy for medulloblastomas and found an initial decline in IQ at 2 years posttreatment, but no evidence of further decline at the 5-year follow-up (Radcliffe et al. 1994). Medulloblastoma is a malignant tumor type and is treated with craniospinal radiation, and thus cognitive impairment from the tumor, dose burden, and malignancy effects are likely comorbid factors. Nevertheless, children with medulloblastoma and late-delayed radiation effects are invariably in need of special supports for learning. In other prospective studies of children with leukemia or medulloblastomas, both of whom received craniospinal doses (doses to whole brain and the spine, in lower doses than those given to targeted tumors, but with a boost to a high dose to the tumor area), declines in IQ were

not limited to radiation effects and were also related to underlying disease (Longeway et al. 1990; Mulhern et al. 1991; Ochs et al. 1991; Rubenstein et al. 1990).

Future Directions

The differential diagnosis of progressive, irreversible late-delayed radiation effects includes the need to differentiate (1) cognitive impairment from tumors versus vascular injury; (2) effects of other clinical factors as effects of the tumor, nonmass neoplasm (such as leukemia), malignancy, and age, for example, which are risk factors for iatrogenic damage; (3) diffuse radiation effects from other disease-related changes in the brain such as from cytokines, inflammation, and chronic pulmonary disease; and (4) changes in imaging studies of radiotherapy effects versus surgical intervention and white matter risks of aging. Thus, it is critical to understand the clinical factors that interact with radiotherapy effects, and their impact on cognitive and radiographic outcomes.

The introduction of proton beam therapy for treatment of many brain tumors, which significantly decreases the distribution and therefore total dose of radiation to healthy brain tissue, is hoped to bring decreases in the functional morbidity of radiotherapy, without loss of, and possibly benefits to, survival rates. The hippocampus neural milieu may be particularly damaged by therapeutic levels of radiotherapy (see “► Radiation Injury”), and other studies are needed to understand its temporal patterns of change, following radiotherapy and its recovery capacity.

Hippocampal protection: New techniques of administering radiotherapy are designed to routinely spare the hippocampus to the greatest degree possible, because of the prominent memory impairment following treatment (Gondi et al. 2010). Techniques also strive to protect other critical structures such as the circle of Willis, optic chiasm and tracts, and the heart. Thus, proton beam promises to provide greater control over the spread of radiation to nontarget areas.

Cross-References

- Early-Delayed Effects of Radiation
- Involved Field Radiotherapy
- Late Effects of Radiation Therapy
- Proton Beam Therapy
- Radiation Injury
- Radiation Necrosis

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- such as a single neuropsychological subtest score or a behavioral rating scale score are observed variables. Such a measure can also be referred to as an *indicator variable*, as it indicates or reflects the latent construct. Whereas a single indicator variable measures one dimension of behavior, the latent variable can collectively explain a wider range of behaviors or processes.
- Some statistical analyses, such as structural equation modeling (SEM), use latent variables as a representation of the shared variance (or covariance) of multiple indicator variables. Although observed measures inevitably entail measurement error, latent variables account for this error and provide a clearer representation of the construct. In factor analysis, underlying latent factors are determined by identifying how individual items or subtests are correlated with each other. In path model diagrams, indicator variables are typically depicted using rectangles and latent variables using circles or ovals.

Current Knowledge

A classic example of a latent variable in the cognitive sciences is Charles Spearman's *g* factor, reflecting general intelligence. Although intelligence cannot be directly measured, performance across a series of standardized intelligence tests is thought to collectively reflect the underlying general intelligence factor, *g*. Even though the individual tasks may be very different, the commonality across their performance scores theoretically represents the global intelligence factor. Subsequent theorists and researchers have proposed sub-factors to general intelligence, such as working memory and fluid reasoning, which are also latent variables.

See Also

- Factor Analysis
- Structural Equation Modeling

Further Reading

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Latent Variable

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Definition

A latent variable represents a construct that is unobserved and not directly measurable. Latent variables are often hypothetical or abstract concepts. In the behavioral sciences, examples of such variables might include quality of life, depression, and selective attention. In contrast, measures

Lateral Gaze Palsy

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Synonyms

Horizontal gaze palsy

Definition

Lateral gaze palsy is an inability to produce horizontal, conjugate eye movements in one or both directions. Lesions of the cranial nerve VI (abducens) nucleus in the pons cause ipsilateral, horizontal gaze palsy by disrupting motoneurons that innervate the ipsilateral lateral rectus muscle by way of cranial nerve VI and interneurons that connect to the contralateral cranial nerve III nucleus in the midbrain, via the *medial longitudinal fasciculus*, to stimulate the medial rectus of the opposite eye. Lesions of the paramedian pontine reticular formation, adjacent to the abducens nucleus, may cause lateral gaze palsy, particularly involving ipsilateral saccadic eye movements. Lesions of the frontal or parietal cortical eye fields may also cause weakness of horizontal gaze (contralateral to frontal lesions and ipsilateral to parietal lesions) that becomes more subtle over time.

Cross-References

- [Internuclear Ophthalmoplegia](#)
- [Oculomotor Nerve](#)
- [Pons](#)

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Lateral Geniculate Nucleus of the Thalamus

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Synonyms

LGN

Structure

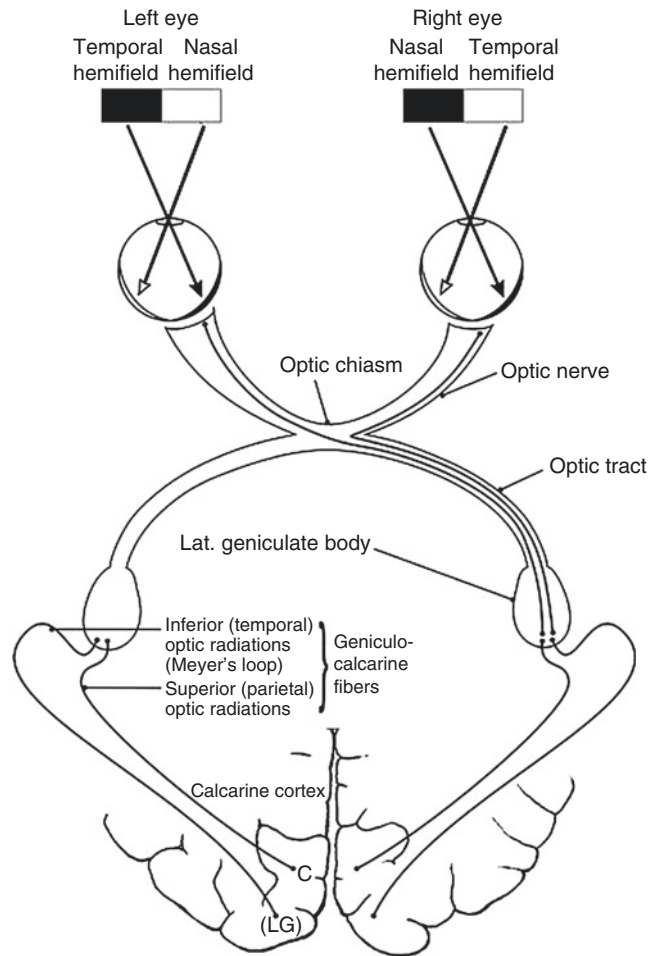
Anatomy and location: The lateral geniculate nucleus (LGN) is a bilateral nucleus located on the caudal, inferior surface of the thalamus, lying lateral to the medial geniculate nucleus, inferior to the pulvinar and superior to the pretectal area. The LGN comprises six layers that relay information to cells in the visual cortex. The magnocellular layers (layers 1–2) send information to the area of the cortex that processes large features and motion. The parvocellular layers (layers 3–6) send information to the area of the visual cortex that processes finer details and color.

Input pathways: Visual input from retinal ganglion cells in both eyes sends information to the optic nerve, whose fibers cross at the optic chiasm and then continue in the optic tract. Fibers cross so that information from the right visual field from both eyes is sent to the left optic tract and information from the left visual field of both eyes is sent to the right optic tract. Optic tract fibers project around the midbrain to reach the LGN.

Output pathways: From the LGN, third-order thalamocortical neurons project through the retrolenticular part of the internal capsule and form broadly spreading fibers called optic radiations, which terminate in the primary visual cortex of the occipital lobe. As the thalamocortical fibers leave the LGN, they are divided into inferior and superior radiations and pass around the lateral ventricle (Fig. 1). Inferior projections (Meyer's loop) follow

Lateral Geniculate Nucleus of the Thalamus,

Fig. 1 Schematic of visual system, including LGN (Mendoza and Foundas 2008)



through the temporal lobe, synapse on inferior areas of the primary visual cortex, and supply information about the superior visual field. Superior projections travel through the parietal cortex, synapse on superior regions of the primary visual cortex, and supply information about the inferior visual field.

Function

The primary function of the LGN is to relay visual information from the retina to the visual cortex.

Illness

Lesions prior to LGN: (a) Disease of the eyeball (e.g., cataract) and disease of the optic nerve (e.g., multiple sclerosis) lead to loss of vision in the

affected eye, **monocular blindness**. (b) Damage to the medial aspect of the optic chiasm/compression of the optic chiasm (e.g., adjacent pituitary tumor) leads to **bitemporal hemianopsia**, the loss of peripheral vision in both eyes. (c) Damage to the lateral aspect of the optic chiasm (e.g., aneurysm of the internal carotid artery) will affect the fibers of the ipsilateral temporal hemiretina (nasal visual field). (d) Damage to optic tract leads to loss of vision in contralateral visual field in both eyes (**homonymous hemianopsia**).

Lesions at or after LGN: (a) **Meyer's loop cut:** lesion to temporal optic radiation leads to contralateral **superior quadrantanopsia**. (b) Lesion to parietal portion of optic radiation leads to contralateral **inferior quadrantanopsia**. (c) Lesion to occipital cortex leads to contralateral

homonymous hemianopsia with **macular sparing** (intact foveal vision).

Cross-References

- ▶ [Magnocellular Neurons](#)
- ▶ [Meyer's Loop](#)
- ▶ [Optic Radiations](#)
- ▶ [Optic Tract](#)
- ▶ [Parvocellular Neurons](#)
- ▶ [Thalamus](#)
- ▶ [Visual Field Deficit](#)

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Lateral Inhibition

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Synonyms

Sensory inhibition; Spatial inhibition

Definition

Lateral inhibition refers to the capacity of excited neurons to reduce the activity of their neighbors.

Neurons that are firing inhibit the stimulation of surrounding. Accordingly, only the neurons that are most stimulated and least inhibited respond. Lateral inhibition plays an important role in visual perception by increasing the contrast and resolution of visual stimuli. This occurs at various levels of the visual system. For example, when a small light is presented in a dark environment, receptors on the retina central to the stimulus are activated and transduce the visual information to the brain, while receptors that are peripheral to the stimulus send inhibitory signals that enhance the perception of darkness in the surrounding. This process has the effect of creating greater dark-light contrast and is responsible for the Mach band visual effect. Similar inhibitory processes occur cortically and contribute to both object and spatial perception.

Cross-References

- ▶ [Cortical Magnification](#)
- ▶ [Enhancement](#)
- ▶ [Perception](#)

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Lateral Lemniscus

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Definition

A pontine-mesencephalic pathway that carries auditory information. Lemniscus means “ribbon”

and anatomically is used to refer to a fiber pathway or tract. The fibers in the lateral lemniscus originate in the cochlear and superior olivary nuclei of the pons and carry both ipsilateral and contralateral auditory information. It terminates in the nuclei of the inferior colliculi in the mesencephalon. The lateral lemniscus should be differentiated from the *medial lemniscus*, another brainstem fiber pathway which carries somatosensory information. Because of the bilateral nature of the auditory pathways, unilateral lesions of the lateral lemniscus are not normally associated with clinically notable hearing losses.

Cross-References

► Auditory System

References and Readings

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Lawton-Brody Instrumental Activities of Daily Living Scale

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Synonyms

Lawton-Brody iADL scale; Lawton iADL scale

Description

The Lawton-Brody Instrumental Activities of Daily Living (iADL) scale covers eight functional domains: using the telephone, shopping, food preparation, housekeeping, laundry, transport,

medication, and finances. Competence is rated according to descriptions of the person's level of involvement/ability in each activity (e.g., for using the telephone, four levels of competence are described: operates telephone on own initiative, looks up and dials numbers, etc.; dials a few well-known numbers; answers telephone but does not dial; does not use telephone at all). It should be administered by a researcher or practitioner with relevant qualifications, with ratings derived from interview, which should take between 10 and 15 min. Activities in which a person has never participated are excluded (e.g., males are not assessed on laundry, meal preparation, and housekeeping if their wife has always taken responsibility for these things), but can also be rated regarding whether a person *could* do them. There are several ways of scoring responses, but Graf (2008) states that common practice is to score each item either on a simple independent/dependent basis, or on a 3-point scale (dependent/needs assistance/independent). Vittengl et al. (2006) reviewed a variety of scoring procedures and found no advantages for more complex over simple scoring systems, and thus advocate the use of simple methods.

Historical Background

The Lawton-Brody iADL scale was developed in 1969 (Lawton and Brody 1969). Despite the lack of good evidence regarding its psychometric properties, it is a very widely used measure.

Psychometric Data

Sikkes et al. (2009) provided a review of ADL scales for people with dementia. Each scale was examined in terms of nine indices of psychometric quality. The Lawton-Brody iADL scale was found to have a positive result in only one index, as there was evidence of good internal consistency for two subscales (Cronbach's alpha between 0.78 and 0.91). However, it should be noted that only 2 of the 12 scales examined achieved two positive results (the Disability Assessment for Dementia and the Bristol Activities of Daily Living Scale). Sikkes

et al. also report that there is an apparent ceiling effect; in that 20% of people with dementia in one study achieved the highest possible score. They report that data for determining construct validity, reliability, and responsiveness were not available.

Vittengl et al. (2006) examined the value of different scoring methods, including whether the scale's predictive validity differed according to the type of scoring procedure used. Their sample comprised 231 people aged on average 78.3 years (SD 11.4), who lived in rural areas of the mid-western USA. Although no significant differences were found between different scoring methods, iADL scale scores were found to be strong predictors of mental status, psychosocial functioning and living situation, moderate predictors of outpatient medical care, and weak (but statistically significant) predictors of depression and inpatient medical care during the preceding month, suggesting the measure is a valid one to use.

Clinical Uses

The scale is useful in determining an individual's level of competence in everyday activities, and consequently, the degree of assistance that may be necessary for the individual to ensure the attainment of an optimum level of functioning. It may also be useful in measuring change over time or with intervention, but the lack of evidence regarding its sensitivity to change may mean that a different or an additional outcome measure should be used for this purpose.

Cross-References

- [Independent Living Scales®](#)
- [Katz Index of ADLs](#)

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Lead Exposure

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Synonyms

Lead toxicity; Plumbism

Definition

Direct or indirect contact with organic or inorganic lead resulting in a harmful alteration of body structure and/or function, including illness or death.

Current Knowledge

Lead is a virtually omnipresent heavy metal that has been reported to negatively affect all organ systems. The neurological effects of lead are particularly pernicious, with architectural changes to or death of neurons in a variety of cerebral areas reported (e.g., hippocampal areas and the amygdala may be targets of organic lead; the cerebellum and hippocampus may be favored by inorganic lead). The nervous system can be affected by lead directly (through alterations in CNS development or pharmacological activity) or indirectly (by impacting other bodily organs or functions, such as the kidneys, that can then affect brain functioning). Lead exposure can be

acute or chronic. Acute lead poisoning is much less common in the United States, as use of lead in plumbing, fuels, food storage, and paint has been reduced and enhanced regulations have lowered the risk of occupational lead exposure. However, persons with low socioeconomic status continue to be differentially exposed to lead acutely. Research indicates that chronic low-level lead exposure is of concern in its own right, particularly with respect to its effect on the neurological development of children.

Children are more sensitive to lead exposure than adults, as they absorb and store lead more readily and tend to ingest greater quantities. Cognitive and neurobehavioral deficits attributed to lead exposure in childhood have been noted to be quite variable. This variability is likely dependent upon when in the developmental/brain maturation process the child is exposed to lead but may also be exacerbated by environmental stressors. High blood lead levels are routinely found to be associated with more severe attentional, intellectual, executive, and externalizing problems in emotional/social adjustment than lower blood levels. However, even very low blood lead levels (less than 5 micrograms of lead per deciliter) have been correlated with lowered intelligence quotients (perhaps in a dose-response relationship), cognitive inflexibility, slower psychomotor reaction speed, and aspects of attentional difficulties. A reduction in blood lead levels over time has not been consistently shown to result in cognitive/behavioral improvement. This may be due to the fact that lead remains in the bone, brain, and other tissues for much longer periods of time than it does in the circulation. Cognitive and behavioral impairments caused by childhood lead exposure appear to remain present to some degree into adulthood and may lead to progressive cognitive difficulties, perhaps even dementing conditions. These and similar findings have resulted in the conclusion that any exposure to lead, no matter how seemingly minimal, is unacceptably dangerous.

Although childhood exposure to lead is deemed to be much more deleterious than adult exposure, a wide variety of neurocognitive deficits have been noted in adults exposed to lead.

Visual-spatial skills and motor functions may be particularly vulnerable to the effects of lead. Psychomotor speed, memory, and executive/attentional abilities are common cognitive functions affected, particularly at higher lead levels. Irritability, dysphoria, sleep disturbances, and other affective symptoms are commonly reported. Psychotic symptoms have been observed as well. Some of the clinical symptom picture may vary with the type of lead (organic versus inorganic), degree of cognitive reserve (i.e., the brain's resistance to cognitive decline), psychosocial stressors, and other factors. Acute lead exposure leads to acute cognitive difficulties, but chronic lead exposure or cumulative lead buildup may be associated with progressive cognitive deterioration. Older adults with a past history of lead exposure are at particular risk for delayed lead-related effects (e.g., due to osteoporosis causing stored bone lead to be re-released into the circulation).

Cross-References

- [Mercury Exposure](#)
- [Toxic Exposure](#)

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Learned Non-use

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Synonyms

Learned motor non-use; Learned non-use of spoken communication

Definition

Observed reduction of a behavior that cannot be exclusively attributed to an impairment in the central nervous system.

Historical Background

Learned non-use was first observed in basic research conducted with monkeys who underwent surgical deafferentation of an upper limb. After deafferentation, researchers observed that when the monkeys used a compromised arm or hand to obtain food, they would do so inefficiently resulting in a form of negative reinforcement. Consequently, in an attempt to become more proficient, the monkeys resorted to only using their unaffected upper limb to climb and eat with relative ease. This positively reinforced the behavior of not using an impaired limb. Since the observed diminished motor movement of the monkeys' impaired limb could not solely be accredited to the surgically induced central nervous system damage, the investigators coined the observed behavior — learned non-use (Taub et al. 1972; Taub 1977, 1980).

Current Knowledge

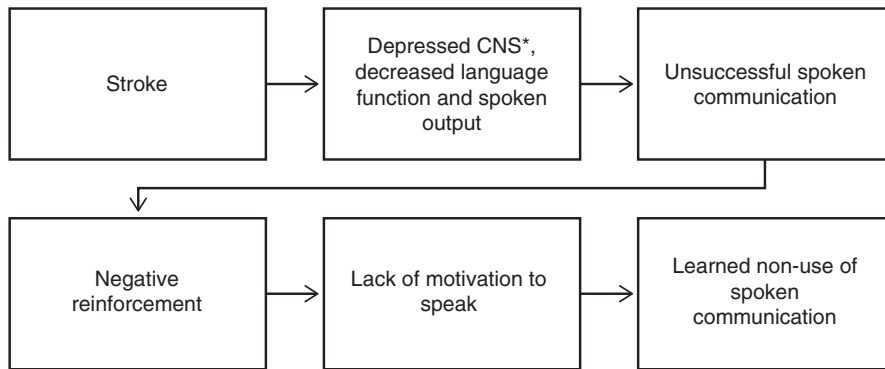
Learned non-use has been translated to human stroke rehabilitation for individuals who acquire motoric (e.g., Gotta et al. 2004) and linguistic

deficits (Ball et al. 2006; Pulvermuller et al. 2001; Szaflarski et al. 2008) post stroke. Therefore, learned non-use pertains to both reduced movement, learned motor non-use, and communication, learned non-use of spoken communication, which are not necessarily concomitant.

Learned non-use is thought to be perpetuated through principles of operant conditioning which suggest that actions are shaped by a series of positive and negative reinforcement (Skinner 1957; Thorndike 1898). Environmentally reinforced behaviors are more likely to become habituated, even behaviors such as learned non-use. Figure 1 depicts the development of learned non-use of spoken communication. A reduction in spoken communication begins with damage to the central nervous system, which causes decreased language function (i.e., aphasia) and impaired spoken language production. These deficits in turn result in unsuccessful communication, which is negatively reinforced by an individual's environment. Negative reinforcement of spoken communication leads to decreased motivation, avoidance of talking situations, and ultimately a reduction of spoken communication overall. Thus, the behavior of learned non-use of spoken communication is established and then perpetuated (see Fig. 1).

Future Directions

Habits of learned non-use may be overcome through intensive therapies (Taub et al. 2006). Constraint-induced aphasia therapy (CIAT) is a language treatment that was specifically designed to help individuals with aphasia overcome learned non-use of spoken communication (e.g., Meinzer et al. 2012; Pulvermuller et al. 2001; Szaflarski et al. 2008). Pulvermuller et al. (2001) were the first to document the application of CIAT with the intention of overcoming learned non-use of spoken communication through the adoption of principles from constraint-induced motor therapy: (a) intensity, (b) constraints, and (c) shaping. Since the seminal article in 2001, many investigations have assessed the efficacy of CIAT, and the treatment has been associated with favorable outcomes on standardized language assessments,



Learned Non-use, Fig. 1 Development of learned non-use of spoken communication adapted from Ball et al. (2006) and Taub et al. (2006). *CNS central nervous system

discourse analyses, and functional communication measures (e.g., Cherney et al. 2010; Meinzer et al. 2012). Forthcoming studies may investigate aspects of the CIAT protocol such as the principles of shaping, intensity, and constraints and/or the social environment created by CIAT to diminish the effects of post-stroke learned non-use of spoken communication.

See Also

- ▶ Aphasia
- ▶ Constraint Induced Therapy

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Learned Treatise

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Synonyms

Authoritative reference

Definition

A learned treatise is authoritative text, which is considered evidence that is provided to support claims. Learned treatise is admissible as evidence in court. Learned treatise can be text that an expert witness used that text to reach his conclusions. Under the Federal Rules of Evidence, either party can introduce a learned treatise as evidence.

Cross-References

► [Federal Rules of Evidence](#)

References and Readings

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Learning

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Synonyms

Acquisition of knowledge; Erudition

Definition

The cognitive process of acquiring a skill or knowledge. A relatively permanent change in performance that results from practice (Logan and Gordon 1997).

Historical Background

The ability to learn is an innate cognitive function possessed by humans, animals, and plants. Learning does not happen all at once but tends to follow a learning curve, building off of previous knowledge (Schacter et al. 2011). Learning is not the same as performance (Soderstrom and Bjork 2015). Learning is how much permanent change in performance occurs over successive learning trials. Therefore, learning is assumed to go on between trials, whereas performance is measured at each trial. Questions such as “What is learning?” or “What is learned?” have been the impetus for many different theories. We begin our discussion of learning with the classical theories, which provide the backdrop to the more recent theoretical discussions of this elusive concept. Table 1 is a summary of these theoretical orientations:

Learning, Table 1 Summary of Theoretical Orientation

Theorist	Tradition	What is learned?	Reward necessary
Pavlov	Connectionist	CS-CR connections	No
Watson	Behaviorism	S-R connections	No
Guthrie	Behaviorism	S-R connections	No
Thorndike	Reinforcement	S-R connections	Yes
Hull	Reinforcement	S-R connections	Yes
Skinner	Reinforcement	S-R reflexes and R-S operants	Yes
Wertheimer	Gestalt	Gestalt whole	No
Tolman	Purposive	Sign-Gestalt expectancies	No
	Behaviorism		

Classical conditioning – Pavlov’s classical conditioning paradigm is central to all theories of human learning. Although Pavlov conditioned dogs to salivate to meat powder, in Western European cultures, classical conditioning has been studied within an eye blink paradigm. In this paradigm, a light brightens just before a puff of air strikes the eye causing the person to blink in response to the air puff. Soon, the person learns to blink as soon as the light changes but before the puff occurs. The puff is the *unconditioned stimulus* and the light is the *conditioned stimulus*. The *conditioned response* is blinking to the light before the air puff (unconditioned stimulus) occurs. Classical conditioning usually does not involve learning any new response or goal-directed problem-solving behavior. Nevertheless, many theorists regard classical conditioning to be the fundamental principle by which we all learn.

Behaviorist theories – John Watson was perhaps the first American to study learning theory. He advocated studying only measurable, objective, and practical behavior. He formalized his thinking in his now famous article *Psychology As The Behaviorist Views It* in 1913. He believed that behavior resulted from conditioned reflexes, and he denied the possibility that we are born with special mental abilities or traits or predispositions to behave in a certain way. He was therefore a strong proponent of the notion that the environment shapes behavior, and he minimized the role of hereditary factors in the development of learned behaviors.

Watson felt that human learning resulted from classical conditioning through which a variety of stimulation comes to elicit the repertoire of reflexes

with which are innate. We are born with these reflexes; however, we are able to modify them and to develop new ones as we grow older. Watson, however, felt that this was only part of the learning process. We learn complex habits by forming sequences of reflexes which accounts for human’s ability to learn complex behaviors. Watson also proposed two basic principles of learning: *frequency* and *recency*. The frequency principle means that the more frequently we have made a given response, the more likely we are to do it again. The recency principle means that the more recently we have made the response, the more likely it is to recur.

Other theorists like Edwin Guthrie (1886–1959) were contemporaries of Watson and were influenced by his behaviorism. Guthrie’s basic principle of learning was “A combination of stimuli which has accompanied a movement will on a future occurrence, tend to be followed by that movement” (Guthrie 1952). In essence, Guthrie felt that the last response a person makes in a situation will be the first one he or she makes in the same situation when it recurs. Guthrie also felt that learning would occur strictly by contiguity, that is, through making the response in the presence of the stimulus even though no reward was present. Reward simply preserved the memory of the last response.

Reinforcement theories – A hallmark of reinforcement theories is that pain and pleasure are consequences of our actions (Bentham 1789). Edward Thorndike (1898) was perhaps the first American psychologist to modify the behaviorist views described above to include the notion of reinforcement as a necessary and sufficient condition for learning. Thorndike’s study of cats led

him to conclude that an animal's ability to learn stimulus and response connections defined what we call *intelligent behavior*. Thorndike, like Guthrie and Watson, believed that learning strengthened with practice. He called this principle the *law of exercise*. However, he also proposed a more important law, which he called the *law of affect*. The law of affect stated that behavior depended on the effect that it produced. If the effect was satisfying, then the learned habit strengthened; if the effect was annoying, then the learned habit weakened (Thorndike 1913, p. 2). Like Guthrie and Watson, Thorndike said nothing about feelings. He simply described a connectionist system that would either enhance or diminish behavior with reinforcement.

Skinner (1938) defined two types of learned behavior. *Respondent behavior* occurred automatically and resulted from specific types of stimulus and response connections that Skinner called reflexes. Respondent behavior followed the laws of classical conditioning. However, Skinner felt that most behavior is not respondent but *operant*. An organism *emits* operant behavior in response to the environment; it is not elicited by any particular stimulus. For Skinner, once operant behavior occurred and was closely followed by reinforcement, the probability that it would occur again increased.

Skinner also distinguished between positive and negative reinforcers. A *positive reinforcer* was something pleasurable that followed the occurrence of an operant, whereas a *negative reinforcer* involved the removal of something aversive following the operant response. Punishment involved the application of something aversive following a response. Skinner's research indicated that punishment did not permanently eliminate behavior. Punishment was ineffective because it was temporary. Skinner found that punished behaviors often would reoccur with even greater frequency later on.

Skinner also developed the notion of *schedules of reinforcement* which referred to the pattern by which reinforcers follow responses. The simplest schedule involved continuous reinforcement, for example, where the reward followed the operant response every time an individual emits the

response. With intermittent reinforcement, the reward followed the response with less frequency. Skinner's research indicated that responding would actually increase with intermittent reinforcement relative to continuous schedules. Moreover, when learning to respond with intermittent reward, the response was even more persistent once the reward was eliminated entirely relative to conditions in which the person initially received continuous reward. Skinner also posited the notion of *shaping* which was the mechanism by which people learn complex behaviors. He considered learning a larger more complex behavior to involve shaping smaller behaviors, a process that he called *successive approximations*.

Reinforcement theories – Clark Hull proposed perhaps the most well-developed connectionist-learning theory of the mid-twentieth century. Like Watson, Guthrie, and Thorndike, his concept of behavior involved the association between stimulus and response. Unlike Skinner, Hull believed that animals and humans never simply emitted a response. The response always resulted from some eliciting stimulus. Hull proposed a four-stage learning process that involved a series of “intervening variables,” that is, unobservable processes that mediated behavior. Hull believed that the values, amounts, and characteristics of the environment determined their effect on the intervening variables, which, in turn, would allow him to predict behavior. In the second stage, Hull defined several intervening variables like *habit strength*, which was the current strength of the learning connection between the independent variables and the desired response. *Drive* was the person's current motivational state. *Reward* provided *drive reduction*. In addition, *inhibition* was the extent to which a person could keep from making a response.

For Hull, reward was necessary for learning to occur. He was also the first theorist of his day to describe the concept of *incentive motivation*. For Hull, learning involved not only an association between a stimulus and a response; it also involved learning that a particular reward was associated with a particular response. Incentive motivation learning was necessary for behavior to occur. Hull's model of learning can be

summarized according to the following multiplicative relationship among his intervening variables.

$$\text{Behavior} = \frac{\text{Habit} \times \text{Drive} \times \text{Incentive}}{\text{Motivation} \times \text{Inhibition}}$$

Kenneth Spence was one of Hull’s students. Spence developed Hull’s theory, especially the notion of incentive. Unlike Hull, Spence assumed that habit strength did not depend on reinforcement. Habit strength would increase whenever a person made the response together with the stimulus that evoked it; however, a person could also learn that different responses produced greater rewards.

Cognitive interpretations of learning – Max Wertheimer started the cognitive revolution in Germany and in the United States. Wertheimer chose the word *gestalt*, which literally means pattern or configuration, to describe human perception and learning. The gestalt psychologists described several different principles of perception. For example, the law of *proximity* described how we perceive items that are close together as a unit. The law of *closure* indicated that our minds seek conclusion and that we seem to perceive partially closed areas as holes. The law *good configuration* indicated that we typically perceive an event in its simplest and most complete form. Unlike the reinforcement theorists, Gestalt theorists did not ask *what has a person learned to do* in terms of stimulus response associations; they asked *how has the person learned* to do it.

Edward Tolman was a cognitive psychologist who was heavily influenced by the gestalt movement. His book *Purposive Behavior in Animals and Man* presented the view that behavior was a response to goals and that an individual is capable of shifting behavior in response to the environment. He also believed that behavior was *molar*, that is, it included large behavioral units that were organized into purposeful goal-seeking strategies. Cognitions involved the amalgamation of several different learning experiences that formed what Tolman called *sign-gestalt-expectations*. In other words, a person comes to expect an organized world that conforms to good configurations. We learn that certain signals or *signs* come to elicit these *gestalt expectations*.

Tolman defined six kinds of learning. *Cathexis* was a tendency to seek out specific goals when experiencing specific drives. *Equivalence beliefs* involved the expectation that the situation will either be rewarding or punishing. For example, giving an employee a pat on the back eventually becomes associated with feelings of acceptance and a job well done. *Field expectancies* were essentially the same thing as sign-gestalt-expectations. Field expectancies are what we call knowledge or mental maps of the environment. *Field cognition modes* are ways that we choose to learn or our desire to learn certain things rather than others. *Drive discrimination* refers to our ability to discriminate or distinguish different motivations. *Motor patterns* included sequences of smaller behaviors that formed larger molar behavior.

Current Knowledge

This combination of theories spawned several others. Table 2 summarizes several of the more recent explanations of learning.

Human Information Processing models describe learning as a computer analogy that involves encoding, consolidation, and retrieval of newly learned information. These models assume that our ability to access information in memory is limited by how well we can encode and consolidate the information. For example, just as we cannot retrieve a file on a computer hard drive

Learning, Table 2 Recent Explanations of Learning

Explanation	What is learned?
Verbal learning	Associations between words and sound patterns
Psycholinguistics	Modification of innate linguistic skills
Concept learning	Prototypes, schemas, exemplars
Human information processing	Mental programs for storing and retrieving information
Mathematical learning	Probabilities for predicting a response
Physiological learning	Neural loops and networks
Learning style	Predispositions to respond

without the file name, information stored in human long-term memory cannot be retrieved unless an appropriate cue is encoded with it at the time it is learned. Just as a computer's central processing unit can defragment/disorganize information on the hard drive to speed up retrieval, the human *executive monitor* consolidates newly learned information in memory to create efficient retrieval. Mathematical learning theory is not a theory per se but a group of algorithms that are capable of predicting certain types of behavior. Physiological learning theory studies the various cellular and biochemical changes in learning that occur within the brain, how different brain structures operate, and how the various structures substitute their activity when another is destroyed.

Learning style refers to behaviors that define ways a person goes about learning new information. For example, many people are *convergent thinkers*, meaning that they use a set of rules to converge upon a solution to a problem. *Divergent thinkers* solve problems with a holistic style in which they try to see the "big picture."

Concept learning is the study of how humans learn categories that divide our environment and domain into examples and non-examples of things we understand. Behaviorist's explanations suggest that we learn concepts through experience and the association of stimuli with responses. The cognitive psychologists define concepts as collections of rules that are generalized in different ways. These rule structures are often referred to as *prototypes* or *schemas*, or the amalgamation of different examples and the abstraction of similarity among them.

Future Directions

Nowhere has learning theory been more prominent than in the field of education. Skinner created the notion of *programmed instructional learning* which was designed to teach difficult and complex concepts by breaking them down into relatively simple components and then rewarding the student for mastery of the components (Lumsdaine and Glasser 1960). The student would seldom make an error because the parts were quite easy to master. Learning the larger concept therefore occurred via *errorless discrimination* (Terrace

1963) and *self-paced instruction* (Skinner 1960). These same principles have been used today in online training programs (McDonald et al. 2005). They have also been used successfully when teaching brain injury survivors (Wilson and Evans 1996). *Self-paced instruction* emphasizes self-regulated learning by monitoring, planning, and adjusting behavior and also has been shown to facilitate concept learning (Rodrigo et al. 2013). Applications of operant conditioning have been used extensively for the management of challenging behaviors in the classroom, as well as after brain injury (Wood and Aldeman 2011). Learning theory emphasizes the fact that forming connections between stimuli and responses requires making the response. Educational learning theorists have formalized this notion as a "learning-by-doing" principle (Reese 2011) which states that learning is maximized when it derives from one's experiences or actions, as opposed to learning from watching others' performance, or listening and reading others' instructions.

Obviously, this account of learning cannot survey all of the important aspects of research in the field. However, this summary of learning has focused on the basic principles and theories that have shaped the development of the field. These theories are important because all of the more recent theories of learning are based on some form of connectionist, gestaltist, or cognitive principles.

See Also

- ▶ [Bender Visual-Motor Gestalt Test II](#)
- ▶ [Cognitive Behavioral Therapy](#)
- ▶ [Concept Learning](#)
- ▶ [Errorless Learning](#)
- ▶ [Retrieval Techniques](#)

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Learning Disability

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Synonyms

Dyscalculia; Dysgraphia; Dyslexia; Dysphasia; Learning disorders

Short Description or Definition

The definition of learning disability has changed over time, but all definitions focus on the idea of academic difficulties that are not expected. According to the DSM-V, a diagnosis of learning disability is assigned when a school-aged child exhibits persistent difficulties in learning and using academic skills, performing below same-aged peers after participating in appropriate efforts to remediate these problems. The child's learning difficulties have a clear negative impact on their academic or occupational achievement or other daily living skills, and the learning difficulties cannot be completely explained by of other possible causes (primary sensory deficit, intellectual disability/other neurologic or mental condition, stressors, poor proficiency in the language of instruction, or poor academic instruction) (APA 2013).

Categorization

Areas of learning difficulty include reading skills, reading comprehension, reading fluency, written expression, mathematics calculation, mathematics problem solving, listening comprehension, and oral expression (Fletcher et al. 2007).

Epidemiology

The number of children with a learning disability in the USA varies based on the definition. Approximately 9% of boys and 6% of girls in the second and third grades have a reading disability (i.e.,

reading achievement is at least 1.5 standard deviations below what would be expected on the basis of IQ score; Peterson and Pennington 2009). Estimated incidence of children with mathematics disabilities ranges from 6% to 14% depending on the definition (i.e., math achievement lower than expected given IQ vs. math achievement lower than expected for grade or age level). Some studies show that math disabilities are more prevalent among girls, but other studies find no gender differences (Barnes et al. 2009). Approximately 39.2% of children between the ages of 6 and 21 who receive special education services in the USA are receiving services for a specific learning disability (U.S. Department of Education 2016).

Natural History, Prognostic Factors, and Outcomes

The etiology of learning disorders is complex, including neurobiological and genetic factors as well as the impacts of home environment and educational instruction (Pennington 2009). Child outcomes may be affected by comorbidity. For example, comorbid mathematics and reading disorders, speech-language disorders, and ADHD may affect child functioning. In addition, children with learning disorders may be vulnerable to internalizing problems that develop in response to the impact of academic failure (Fletcher et al. 2007). Research suggests that learning disorders are persistent, with most persons diagnosed during childhood continuing to exhibit the core components of learning disorders in adulthood.

Neuropsychology and Psychology of Learning Disorders

Children with learning disorders are a heterogeneous group, exhibiting weaknesses in underlying cognitive skills that may vary depending on whether the child is diagnosed with a reading disability (e.g., phonological processing, rapid naming, verbal memory, and language), a mathematics disability (e.g., attention and semantic memory), or a disorder of written expression (e.g., fine

motor skill and language) (Fletcher et al. 2007). Learning disorders such as reading disabilities are associated with externalizing behaviors, especially in boys. Internalizing behaviors, such as dysthymia, low self-esteem, and depressed mood, are associated with reading disabilities in girls (Peterson and Pennington 2009). Children with learning disabilities often have difficulty with attention, motivation, and self-regulation (Barnes et al. 2009).

Evaluation

The process of evaluation for learning disabilities is complicated by frequent changes in how learning disabilities are defined, and the evaluation approach taken depends on the definition subscribed to by the evaluator. Historically, evaluation for learning disability involved identification of children who performed more poorly on tests of academic achievement than was expected on the basis of their measured intellectual ability. However, research suggests that these children do not differ in core academic skills, response to treatment, or outcome from children who exhibit low academic achievement that is consistent with their intellectual functioning in core academic skill deficits, response to treatment, and prognosis (Barnes et al. 2009; Peterson and Pennington 2009). One option for addressing this concern is to diagnose both children who exhibit low achievement and those with a significant discrepancy between IQ and academic achievement with a learning disability (Peterson and Pennington 2009). Alternatively, some authors suggest a response to intervention (RTI) approach, where unexpected academic underachievement is defined by a lack of response to empirically supported classroom instruction (Fletcher et al. 2007). However, there is not a consensus for this approach and it continues to be hotly debated (Reynolds and Shaywitz 2009). In addition, some authors advocate evaluation of underlying neuropsychological processes in order to individualize treatment (e.g., Naglieri et al. 2009). Regardless of definition, there is an emerging consensus about the core academic and cognitive competencies associated with learning disabilities

that can be used to guide evaluations, and the reader is referred to entries on dyslexia and non-verbal learning disabilities for more information.

Treatment

Empirically supported interventions continue to emerge in the area of learning disabilities, with interventions in dyslexia leading the way, followed by interventions in math and written expression (NICHD 2000; What Works Clearinghouse at <http://ies.ed.gov/ncee/wwc/>). Based on an overview of these interventions, Fletcher et al. (2007) offer ten overarching principles for the treatment of learning disorders that emphasize academically focused interventions that increase the time spent on academic work using systematic educational programs that teach content and meta-cognitive skills (e.g., self-monitoring).

Cross-References

- [Dyscalculia](#)
- [Dyslexia](#)
- [Nonverbal Learning Disabilities](#)

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Legal Competency

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Synonyms

Competency to proceed

Definition

Otherwise referred to as “competency to proceed,” this term refers to a criminal defendant’s capacity to participate effectively and make decisions on his or her own legal behalf while being prosecuted. It is to be distinguished from legal sanity because it has a very different legal standard. Furthermore, competency most commonly deals with current mental states (at the time of the proceedings), whereas insanity deals with the mental state (*mens rea*) at the time the offense(s) were committed. Competency to proceed is relevant to any portion of the process, from talking to police (i.e., Miranda rights to remain silent) to plead guilty, receive a sentence, waive one’s right to counsel, and even being executed.

The rationale for questioning/examining a defendant's competency can be traced back to English common law and the seventeenth century. In *Dusky v. United States* (1960), the US Supreme Court upheld the right of a criminal defendant to be deemed competent through the criminal proceedings. Therefore, it would be considered a denial of due process when an incompetent person is tried for a crime, because, by definition, an incompetent person is one who cannot assist counsel and cannot adequately participate in the legal process. *Dusky* set the standard for competency in criminal matters in a two-pronged fashion: (1) the defendant must have the capacity to understand the criminal process he or she is facing (which includes an understanding of the roles of the various participants, such as the judge, jury, and prosecutor), and (2) the defendant must be capable to participate in that process through consulting with counsel in the preparation of his or her defense. Both of these prongs require a *rational* as well as a *factual* level of understanding.

The following represent the specific competencies to be addressed during the criminal justice process: competency to (1) confess (or to waive rights at pretrial investigations), (2) plead guilty, (3) waive right to counsel, (4) stand trial, (5) be sentenced, (6) waive further appeal (when facing execution), and (7) be executed. Forensic psychiatrists and forensic psychologists (more often than neuropsychologists) can play a critical role in the assessment of each type of specific competency by conducting a comprehensive interview and via the administration of several empirically validated instruments specifically designed to assess various aspects competency. Neuropsychologists are more likely to become involved in competency assessments when a defendant claims amnesia, when there is a suspicion of dementia or a recent head injury, or when other neurological illness(es) that could impair the defendant's cognitive abilities underlying competence are at issue. Neuropsychologists bring their specialized knowledge of the science of brain-behavior relationships and the impact of cognitive impairment on functional abilities and their expertise in detecting non-credible self-presentations (e.g., feigning, malingering). In this way, the neuropsychological examination may be a

very valuable addition to the assessments provided by other professionals in assisting the trier of fact in criminal forensic settings.

Cross-References

- ▶ [Capacity](#)
- ▶ [Criminal Responsibility](#)
- ▶ [Diminished Responsibility](#)
- ▶ [Dusky v. United States \(1960\)](#)
- ▶ [Estelle v. Smith \(1981\)](#)
- ▶ [Insanity](#)
- ▶ [Insanity Defense](#)

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Leiter International Performance Scale, Third Edition

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Synonyms

Leiter-3

Description

The Leiter International Performance Scale – Third Edition (Leiter-3) (Roid et al. 2013) is a widely used measure of nonverbal intellectual functioning that consists of both perceptual and conceptual tasks designed to measure aspects of attention, cognition, and memory. It is administered without vocal instructions and does not require verbal responses, although examinees may employ verbal mediation on some items.

The Leiter-3 has two primary domains, a Cognitive battery made up of five subtests assessing nonverbal intellectual functioning and an Attention and Memory battery comprising five subtests. The latter battery is intended to aid in neuropsychological assessment and differential diagnosis for individuals suspected of attentional difficulties, learning disorder, or who have experienced a traumatic brain injury. For individuals with severe cognitive impairments, the measure also allows for the calculation of a Growth Score to compare results and small changes in scores over successive administrations.

Administration of the Cognitive battery takes approximately 20–45 min to complete, depending on whether all subtests are administered (calculation of the Nonverbal IQ score only requires four of ten subtests). Subtests have different start points based on the individual's age (e.g., 3–5, 6–10, and 11–75+).

Historical Background

The roots of the Leiter-3 are found in the work of Russell Graydon Leiter who, in 1927, began developing a measure of intelligence that would have applicability across cultures. The forerunner of the original Leiter International Performance Scale was published in 1929 as a part of his Master's Thesis. In 1940, the first commercial edition was published with 68 subtests that covered the ages of 2–18. The Leiter was revised in 1997, and was standardized on over 2,000 children and adolescents covering the ages 2–20 years and 11 months. In addition to changes in test materials (e.g., colored cards instead of blocks, easels), the revised version (Leiter-R) utilized

more sophisticated psychometrics such as item-response theory (IRT) and linear structural relations (LISREL) in its development. The most recent revision (Leiter-3) was published in 2013 and was standardized on a normative sample of 1603 individuals using continuous norming procedures. The development of the Leiter-3 also used IRT item analysis, and employed the Rasch model to comprehensively examine item characteristics. Additional changes to the Leiter-3 included a reduction in the number of subtests from 20 to 10, and the inclusion of more hands-on materials, such as block-and-frame format and foam manipulatives.

The theoretical underpinnings of the Leiter-3 lie in hierarchical models of cognitive skills hypothesizing an overall general ability termed *g* (e.g., Carroll 1993; Gustafsson 1984), and the Cattell-Horn-Carroll theory of cognitive abilities (CHC theory; cf. McGrew and Flanagan 1998). The CHC theory posits *g* at the highest hierarchical level above a range of other cognitive abilities, including fluid, crystallized, quantitative, short- and long-term memory; auditory processing speed; decision speed; and language development. The Leiter-3 battery is based on this hierarchical model, and yields an estimate of overall intelligence, or *g*, from two of these factors: fluid reasoning and visualization. The remaining CHC factors assessed by the Leiter-3, attention and short-term memory, are used as clinical indicators rather than components of general ability.

Psychometric Data

The Leiter-3 results can be reported as standard scores (such as traditional IQ scores), scaled scores, and percentiles. Using a standardization plan based on the 2008 and 2011 US Census statistics, the Leiter-3 was standardized on 1603 individuals from the general population and 300 individuals from 12 different clinical groups, including: Severe Speech/Language Impairment, Deaf or Hard of Hearing, Severe Orthopedic or Motor Delay or Deviation, Traumatic Brain Injury, Significant Intellectual Deficiency, Attention Deficit Hyperactivity Disorder (ADHD) with

and without Hyperactivity, Gifted, Learning Disability – Reading Disorder, Learning Disability – Other, English as Second Language – Spanish, English as Second Language – Asian or Other, and Autism Spectrum Disorder. The Leiter-3 manual reports internal consistency reliability ranging from 0.88 to 0.93. Evidence for concurrent validity includes strong correlations between Leiter-3 nonverbal IQ score and nonverbal index scores from the Leiter-R ($r = 0.78$), the Stanford-Binet Intelligence Scale, Fifth Edition ($r = 0.77$), the Wechsler Intelligence Scale for Children – Fourth Edition ($r = 0.73$), and the Wechsler Adult Intelligence Scale – Fourth Edition Perceptual Reasoning Index ($r = 0.72$). Confirmatory factor analyses support the Leiter-3 fitting, a hierarchical g model of cognitive abilities.

Clinical Uses

Proponents of the Leiter-3 suggest that its format and development emphasize the measurement of “fluid intelligence,” considered a more reasonable measure of innate intellectual ability, given its lack of vulnerability to educational, social, and other influences. Other advantages include the covered age range (3 years 0 months to 75+ years) and the large range of standardized IQ scores, from 30 to 170.

The Leiter-3 has another advantage in its nonverbal administration and lack of dependence on verbal responses, allowing for the assessment of intellectual functioning when difficulties with language or hearing could be a potential source of confound. The authors of the measure suggest its appropriateness for individuals with hearing impairments, expressive or receptive language disorders, learning disabilities, cognitive impairment, traumatic brain injury, English as a second language, attentional problems, and autism spectrum disorder. Researchers have demonstrated its utility in assessing cognitive abilities of children with Fragile X (Hooper et al. 2000), language impairment (Farrell and Phelps 2000), and autism (Tsatsanis et al. 2003).

Some researchers have voiced a concern regarding Leiter-3 administration, noting that a

number of children found it unusual for the examiner to remain silent throughout the administration. Standardized administration allows for some conversation before and in between subtests, primarily to establish and maintain rapport. Tsatsanis et al. (2003) found very brief vocalizations (“touch,” “point”) to be effective for the population they assessed, which were children with low-functioning autism. Tager-Flusberg et al. (2016) also described similar administration modifications, including brief verbal instructions (“just one” or “match”), when testing children with autism to account for their difficulties understanding nonverbal gestures and maintaining attention.

Cross-References

- ▶ [Stanford-Binet Intelligence Scales and Revised Versions](#)
- ▶ [Wechsler Intelligence Scale for Children](#)
- ▶ [Woodcock-Johnson IV](#)

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Lennox-Gastaut Syndrome

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Synonyms

Childhood epileptic encephalopathy with diffuse slow spike and waves

Definition

Lennox-Gastaut syndrome (LGS) is characterized as a severe epileptic encephalopathy with generalized seizures of multiple types that emerge in children between the ages of 1 and 8 years and occur with high frequency. EEG studies typically reveal an abnormal background with slow spike-and-wave activity that occurs at less than 2.5 Hz frequency. Prognosis is poor, and intellectual disability is traditionally considered a defining feature.

Epidemiology

Approximately 1–4% of childhood epilepsy cases are believed to meet the criteria for LGS. This accounts for about 10% of epilepsy syndromes that begin during the first 5 years of life. The

prevalence rate in Western countries ranges from 0.1 to 0.28 per 1000, and about 2 in every 100,000 children receive a diagnosis of LGS each year. Representation among children with intellectual disability is higher and is estimated to be about 7%. Among institutionalized patients with moderate-to-severe intellectual disability, the percentage is estimated to be as high as 16.3%. Males are believed to be at higher risk for LGS, but this is not consistently supported in the literature. There do not appear to be differences in the prevalence of LGS among geographic regions or ethnicities.

Natural History, Prognostic Factors, and Outcomes

Age of onset in LGS is between the ages of 1 and 8 years, with most cases emerging in preschool age or later (3–8 years). Peak incidence occurs between 3 and 5 years of age. LGS can be either idiopathic or symptomatic, with symptomatic cases being much more common (70–78%). Among these, brain malformations, hypoxic-ischemic insult, encephalitis, meningitis, and tuberous sclerosis are the most common etiologies. Patients with brain lesions are more likely to have abnormalities in the frontal lobes than any other brain regions. LGS secondary to brain tumor or metabolic disorder is rare. Up to 44% of patients with LGS have been described as being cryptogenic (i.e., cause is suspected but cannot be determined). Family history of epilepsy is reported in 3–27% of cases, and it is more common in the subset of patients with cryptogenic LGS (48%).

Multiple seizure types develop in children with LGS and most frequently include tonic, atonic, myoclonic, and atypical absence seizures. Daily seizures are typical and are persistent in 60–80% of cases. While the course of the condition can vary, prognosis in LGS is poor. Intellectual disability is evident in 20–60% of cases prior to diagnosis, and cognitive stagnation and/or deterioration is observed in the majority of cases. Within 5 years of diagnosis, an estimated 90% of cases meet diagnostic criteria for intellectual disability. Risk factors for severe intellectual

disability include the following: younger age of onset (<3 years), nonconvulsive status epilepticus, previous history of West syndrome, and symptomatic etiology. More frequent episodes of status epilepticus are associated with poorer functional outcomes. Children with atypical absence seizures or myoclonic seizures may have a relatively better prognosis.

About half of patients will continue to exhibit typical features of LGS 10 years after diagnosis. While 15.5–23.5% of patients may experience resolution of the characteristic features of LGS, they typically experience ongoing severe, multifocal epilepsy. Very few patients with LGS achieve seizure freedom. Youth with LGS demonstrate an associated mortality rate of 5–17% during follow-ups of 12–21 years (Autry et al. 2010). However, even among patients who experience seizure freedom, cognitive impairment usually persists.

Neuropsychology and Psychology of Lennox-Gastaut Syndrome

LGS is associated with severe and persistent cognitive impairment. Intellectual disability is apparent in the majority of cases within the first 5 years of the diagnosis, and cognitive impairment becomes more prominent over time. This appears to be mediated by age of onset, with cognitive impairment documented in about 98% of cases with seizure onset before age 2 years and 63% of cases with seizure onset after age 2 years. The mechanism of cognitive impairment appears to be related to a combination of developmental stagnation related to slower EEG background rhythm and frequent epileptic activity or cortical degeneration in the case of status epilepticus. While cognitive impairment has been well documented in LGS, most studies only report IQ performance.

In a longitudinal study completed by Oguni et al. (1996), about 68.8% of patients with LGS were functioning in the mentally impaired range at their first visit, with no significant difference between cryptogenic and symptomatic cases (67% and 70%, respectively). By the time of their last visit, 98.6%

of patients with LGS were functioning in the mentally impaired range. While rates of mental impairment among cryptogenic and symptomatic patients were similar at follow-up (95% and 100%, respectively), patients with symptomatic LGS had higher rates of severe or profound intellectual disability (76%) than patients with cryptogenic LGS (43%). This difference, however, was likely partially accounted for by a higher rate of severe intellectual disability in patients with symptomatic LGS at the time of the first visit (38%). Over a mean interval of about 17 years, Oguni et al. reported a decrease of greater than 14 IQ points in 82% of patients with cryptogenic LGS and 78% of patients with symptomatic LGS.

Kim et al. (2015) reported that 94.7% of their sample of 68 LGS patients had moderate-to-severe intellectual disability 19 years after onset. Twenty-five percent required support for ambulation, and 60.3% required assistance for daily living. Conversely, Yagi (1996) reported in a sample of 102 patients that nearly 12% held full-time employment and were fully integrated into society at 16-year follow-up.

Behavioral disturbance is common in LGS and frequently includes attention problems and behavioral dysregulation. Patients often exhibit hyperactivity, impulsivity, aggressiveness, and poor mood regulation. Social maladjustment is common, but it may be consistent with intelligence level. Older children and adolescents may be at risk for psychosis and social isolation. Autistic features have been associated with LGS, though not consistently. Due to the high frequency of the epileptiform abnormalities in LGS, patients may present in a somewhat obtunded state that interferes with their ability to interact with their environment.

Evaluation

Approximately 20–30% of children with LGS present with a history of being neurologically normal, but a preexisting history of encephalopathy, epilepsy, or other neurological disorders is

common. About 30–41% of patients present with a history of West syndrome, most commonly symptomatic West syndrome.

A number of seizure types are associated with LGS. The most common are tonic seizures (55–92% of cases). The tonic seizures frequently occur during sleep and can vary in their motor involvement. They can be axial tonic (primary involvement of neck flexors and facial muscles), axorhizomelic tonic (additional involvement of the extremities with arm elevation or abduction), or global tonic (additional involvement of distal extremity muscles). Global tonic seizures can lead to sudden falls and may make LGS difficult to distinguish from myoclonic-astatic epilepsy (MAE). However, in contrast to LGS, MAE is predominantly genetically determined, is not associated with West syndrome, and typically has better developmental outcomes.

Atypical absence seizures occur in most patients with LGS (17–60% of cases). Identification of atypical absence seizures can be difficult because they can have a gradual beginning and end that may not be observed by caregivers. Moreover, they can be associated with an incomplete loss of consciousness that allows the patient to continue activities during the ictal period. Episodes of nonconvulsive status epilepticus are common in LGS and can persist for days or weeks. During this time, the patient may alternate between tonic seizures and periods of confusion that may include myoclonic activity of the face or extremities.

LGS can also be associated with atonic, myoclonic, and myoclonic-astatic seizures. Generalized tonic-clonic seizures occur in about 15% of cases, and complex partial seizures have been reported in about 5% of cases.

Imaging studies are an important component of the evaluation in LGS to determine if the etiology is symptomatic. This can better define the potential prognosis and may help guide treatment.

The characteristic EEG profile in LGS involves generalized slowing of all background activity and 0.5–2.5 Hz generalized spike and slow waves interictally when awake. Spike and slow wave activity is described as “slow spike and

waves” due to their frequency (0.5–2.5 Hz) and may be associated with atypical absences. Multifocal interictal epileptiform abnormalities and bursts of activity followed by attenuation may occur during sleep.

Treatment

Seizure management in LGS is difficult and can involve different approaches, such as antiepileptic medications, surgery, dietary modifications, or other treatments. Antiepileptic medications are typically first-line treatments, and valproic acid tends to be the medication of first choice when surveying physicians in the United States and Europe. Lamotrigine or topiramate is typically tried next. Felbamate, lamotrigine, topiramate, rufinamide, and clobazam all demonstrate efficacy in randomized, double-blind, placebo-controlled trials. Polytherapy is a frequent necessity but can be associated with a greater negative impact on quality of life (e.g., sedation, neurotoxicity, etc.).

Surgical management of LGS is sometimes considered in patients with intractable seizures that are particularly severe. The most common surgery for LGS is corpus callosotomy, which is particularly effective at reducing drop attacks. Complete seizure control from surgery is rare, and corpus callosotomy is considered to be palliative. Vagus nerve stimulation (VNS) has also been found to be an effective means for reducing seizure frequency (58% reduction) and drop attacks (81% reduction) in LGS.

The ketogenic diet has been used to help manage seizures in LGS, and reports of its efficacy have been mixed. However, a retrospective review of 71 children with LGS who had the ketogenic diet through Johns Hopkins revealed efficacy after 6 months resulting in 50% seizure reduction in half of the patients, 90% reduction in 23%, and seizure freedom in 1%. Efficacy was similar at the 12-month follow-up (Lemmon et al. 2012). Other benefits of the diet have been reported to include improved behavior, increased stamina, and the need for fewer antiepileptic medications (Table 1).

Lennox-Gastaut Syndrome, Table 1 Lennox-Gastaut syndrome

EEG signature	Slow spike-and-wave activity (<2.5 Hz). May have burst followed by attenuation during sleep and multifocal spike-and-wave activity
Age of onset	3–8 years
Clinical features	High seizure frequency Status epilepticus is common MRI may be normal (idiopathic/genetic or cryptogenic) or abnormal (symptomatic). Cerebral atrophy may be present
Treatment	AEDs: valproic acid, lamotrigine, topiramate, felbamate, clobazam, rufinamide Non-pharmaceutical: ketogenic diet Surgery: vagus nerve stimulator or corpus callosotomy may be palliative options. Resective surgery may be an option in symptomatic LGS
Response to treatment with AEDs	Poor
Seizure freedom	Poor
Functional outcome	Poor (global cognitive impairment is typical)

See Also

- ▶ [Encephalopathy](#)
- ▶ [Myoclonic Epilepsy in Infancy](#)
- ▶ [Status Epilepticus](#)
- ▶ [West Syndrome](#)

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Lesion Burden

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Synonyms

Brain injury; Brain lesions; Disease burden;
Lesion load; Volume loss; White matter lesions,
WML

Definition

Lesion burden, a phrase sometimes used interchangeably with lesion load, is a term that may be similar to the idea in medicine of disease burden but in the neuroimaging literature often refers to the overall cumulative effect or burden of brain lesions identified by magnetic resonance imaging (MRI).

Current Knowledge

Lesion burden has been studied extensively in the field of multiple sclerosis (MS) and typically refers to white matter lesions (WML). Studies in MS may analyze both T1- and T2-weighted MRI identified lesion burden, for example, as well as concomitant brain volume, as they are associated

with clinical outcomes such as health-related quality of life (Mowry et al. 2009), cognitive dysfunction (Patti et al. 2015), and even fatigue (Tedeschi et al. 2009, 2007). The idea of lesion burden or load has also been used with other populations such as stroke in terms of outcome related to speech (Marchina et al. 2011) and motor performance (Zhu et al. 2010). Research in traumatic brain injury has also loosely used this term, though often referring to atrophy (i.e., volume loss) which is a direct result of lesion volume, to predict outcome (Bigler and Stern 2015). Finally, associations between lesion load and mood and cognition have been studied in aging and dementia (Mueller et al. 2010).

See Also

- Dementia
- Functional Capacity Evaluations
- Memory
- Multiple Sclerosis
- Neuroimaging
- Normal Aging
- Severe Brain Injury
- Stroke

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Lesion-Symptom Mapping

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Synonyms

Computerized axial tomography (CAT); Computerized tomography (CT); Digital brain images; Functional network outcomes; Grayscale values; Magnetic resonance imaging (MRI); Pixel; Voxel

Short Description or Definition

Voxel-based symptom lesion mapping (VSLM) uses modern digital imaging technology and software to provide better visualization of where focal pathology is located in the brain related to cognitive and behavioral outcomes in individuals who have experienced a stroke, brain tumor, infection, traumatic brain injury, or some type of neurodegenerative changes that have resulted in focal

damage. This new technology is also used to help localize the importance of focal pathology in influencing functional network outcomes in brain injury patient populations (Abbott et al. 2012; Bates et al. 2003; Callaert et al. 2014; Choi et al. 2012; Dronkers et al. 2004; Genovese et al. 2002; Geva et al. 2012).

Current Knowledge

It is hard to imagine the world today without a television or computer screen. In the twenty-first century, television and computer screens are interchangeable, but it was not always this way. Computed tomography (CT) was originally introduced as *computerized axial tomography* (CAT) scanning in the early 1970s and capable of paper print out displaying Hounsfield units – named after the creator of this imaging technology, Godfrey Hounsfield (see Hounsfield 1973). Hounsfield units (HU) were based on the inferred tissue density measured by the speed of an x-ray beam passing through the tissue. Denser structures like bone slowed down x-ray beam transit with other tissue types also distinguishable by their influence on x-ray beam transmission. Because of these differences, a “picture” printout of a single axial slice of the brain could be generated on paper by aligning the Hounsfield units (numbers) assembled by projecting the beam from multiple angles. Hounsfield units were then transformed for image presentation on x-ray film. As such, the original black and white *image output* of the CAT scan of the brain came only as a hard copy radiographic film or was a *photograph* of the computer screen taken by a Polaroid camera!

As photography moved toward digital format versus film exposure, the black and white display on the computer screen, using a 256-point grayscale that ranged from the whitest white to the darkest black, became central to displaying of CT neuroimaging. In CT imaging, this range was from solid bone (white) to the darkest dark or air (black). Since gray matter (with tightly held cell bodies) has a different x-ray beam density than the myelin-coated axons that distinguish white matter – with both distinctly different than

subarachnoid and ventricular spaces filled with cerebrospinal fluid (CSF) – this 256-point display, with these different grayscale values, emerged as a picture of the brain.

The individual elements that code the grayscale information are known as “pixels.” The term “pixel” is a shortened name for “picture element” and represents the basic programmable unit on a computer display. By knowing the dimensions of a single pixel, then a three-dimensional (3-D) space can be defined. For example, whether considering CT or magnetic resonance imaging (MRI), if the “slice” thickness of a flat two-dimensional (2-D) image of the brain was 1 mm thick, the individual pixels creating that image reflect the grayscale intensity for each 1 mm pixel at every point on the screen. For volume (abbreviated as “vo”) calculations, one needs the dimensions of the picture elements or pixels (abbreviated as “el”), to be used. Since in mathematics “x” is the multiplication sign or signifies “by,” putting these abbreviations together – “vo” x “el” – resulted in the term “voxel.” Accordingly, if the 2-D image is based on 1 mm pixels displayed, but the next slice in either direction is contiguous and is also 1 mm thick, a voxel defined as being constituted by pixels that are 1 mm³, then volume can be computed. Note that on the boundaries of white, gray, and CSF matter, any pixels that straddle the edge will have intermediate values and not necessarily appear distinct for one particular tissue type. At the voxel level, this is the problem of partial volume effect and reflects the loss of contrast between regional tissue and/or fluid differences. Presence of partial volume effects may affect the accuracy of volume estimation and size of a region of interest (ROI).

Both in research and clinical settings, there is an additional classification issue – where an abnormality may reside. If there is a “lesion” (i.e., stroke, tumor, contusion from a traumatic brain injury (TBI), etc.), then an additional distinction must be made regarding what is normal versus abnormal tissue, based on pixel identification. This is partially remedied by algorithms that utilize coordinate information (e.g., Talairach coordinates, see https://en.wikipedia.org/wiki/Talairach_coordinates; or Montreal Neurological

Institute (MNI) Coordinate System, see https://en.wikipedia.org/wiki/MNI_Coordinate_System), examine neighboring voxels, and then create likelihoods that a particular voxel is classified as either gray matter, white matter, lesion, CSF, bone, or a blood vessel.

Capitalizing on these differences, Ashburner and Friston (2000) introduced the technique referred to as voxel-based morphometry or VBM (see ECN section for more information on this). This technique was designed primarily as a whole brain analysis procedure to examine for regional difference. However, those in the field of neuropsychology, especially given its historical routes, were always interested in the influence of a particular *localized* lesion. Indeed, as mentioned above, disorders like stroke, tumor, and even TBI, often resulted in a focal lesion. By identifying just the voxels associated with a lesion, or the location of abnormal tissue within a ROI, the voxel-based symptom lesion mapping (VSLM) provides a method where patients with similar types of pathologies can be group analyzed. With this, not only can lesion overlap be determined, but also the relations of regional voxel differences can be mapped in conjunction with neuropsychological functioning (Bates et al. 2003).

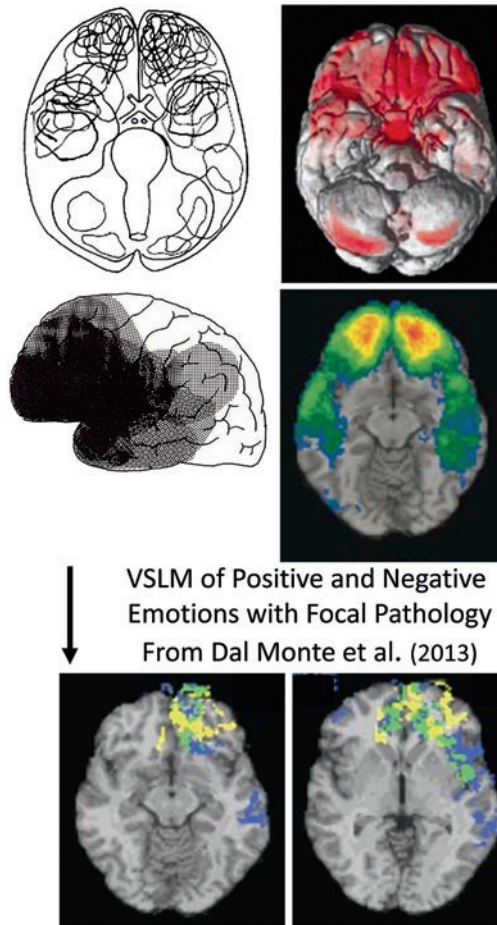
In the very beginning of neuropsychology, there was only the postmortem examination. For example, in the study of focal lesions associated with TBI and prior to contemporary neuroimaging, only the outward description of where a skull fracture was or the position of a penetrating injury could be given, like that, which occurred with Phineas P. Gage (see Thiebaut de Schotten et al. 2015). Figure 1 (upper left) shows the line drawings of Cyril B. Courville, M.D., in the 1960s (Courville 1962), as compared to more modern neuroimaging results in TBI (Dal Monte et al. 2013; Yeates et al. 2007). These line drawings depict where the most common areas of contusions were located in the brain at autopsy from a large sample of individuals who died from their TBI. Of course, not knowing any of this during their ante-mortem state was helpful neither for understanding their neuropsychology nor for relating brain pathology to behavior in the living

individual. Even with the advent of CT imaging, the first in vivo methods were not sophisticated and basically replicated what was previously done at postmortem, by placing an outline of the location of contusions on a line-drawing of the brain derived from looking at CT images, as also shown in Fig. 1 (middle left) from Bigler et al. (1981).

Although Courville's (1962) line drawings only illustrated the ventral view of the brain, it is still clear that the frontal and temporal lobes were/are the most likely areas to be damaged in a TBI. Note how close these line drawings of post-mortem analysis match the outlines made in living individuals with a history of TBI-related contusions, where the line drawings were based on hand "tracing" so the hemorrhagic contusion could be visually identified on CT imaging. With the development of VBM, all of this analysis could be more accurately displayed and performed with automated software techniques. However, one must note that neither the original postmortem, hand-drawn outlines of CT observed contusions, nor the VBM analysis yet provides an easy method for identifying the centroid of where the greatest focal pathology overlaps among those examined – nor do they indicate the frequency of those lesions.

Currently, using a VSLM approach, as shown by Dal Monte et al. (2013) in Fig. 1 (center right), a "heat map" displays where the greatest amount of focal pathology is located in the TBI patient. However, the real benefit of VSLM mapping comes by linking voxel-by-voxel, the relationship of neuroimaging-identified pathology to some neuropsychological variable. For example, in the Dal Monte et al. (2013) investigation, they examined the response to pleasant and unpleasant emotions, as shown at the bottom of Fig. 1. Despite the fact that the greatest overlap of focal pathology was in the anterior frontal area bilaterally (see Fig. 1, right central image), VSLM demonstrated that the relations to emotional perception of pleasant versus unpleasant were associated more with lateralized pathology, not necessarily bilaterally, even though at the group level, the damage was bilateral frontal.

As such, with the VSLM approach, more clinically related information can be extracted from where focal damage is located in the brain and has become a widely used approach in neuropsychology



Lesion-Symptom Mapping, Fig. 1 (Upper Left) Base of the brain schematic where Courville (1962) outlined the general location of surface contusions in fatal injuries involving traumatic brain injury (TBI). (Upper Right) Magnetic resonance imaging (MRI) study of TBI patients that used a voxel-based morphometry (VBM) approach to identify where the greatest amount of difference was in concentration of gray matter voxels in TBI patients with a history of day-of-injury contusion (Figure is adapted from Yeates et al. 2007, with permission from the American Psychological Association). Note that just as was shown by Courville's approach, automated image analysis techniques, using VBM, show that the vulnerability of the frontotemporal regions and inferior surface of the cerebellum are the regions where the greatest pathological changes occur. (Middle Left) Line drawings from the early days of CT imaging that outline the general location of cortical damage in adult patients with TBI (see Bigler et al. 1981). Note how even though this in vivo approach was a crude, time-consuming one; it approached what

Courville showed at autopsy. (Middle Right) This is an automated "heat map" generated from MRI where, using a voxel-based approach, the location of the greatest amount of overlapping damage can be outlined and depicted. As the colors increase toward "warm" (yellow to orange) and to "hot" (orange to red), then greater overlap is indicated. (Bottom Left and Right) Even though the focal damage indicates as bilateral in this voxel-based symptom lesion mapping (VSLM), when it came to processing emotional stimuli, a clear lateralized difference emerged with conjunction analysis between pleasant and unpleasant emotions: Green shows brain structures that overlap between pleasant and unpleasant emotion conditions. Yellow shows lesion-deficit areas unique for unpleasant emotions. Blue shows lesion-deficit areas unique for pleasant emotions. (In each slice, the right hemisphere is on the reader's left.) Note that despite the focal lesions being bilateral, the relations with emotional states are more lateralized and regionally dependent (Used with permission from Dal Monte et al. 2013, and Oxford University Press)

(Geva et al. 2012; Pustina et al. 2017a, b). However, to date, this type of approach typically uses but a single MRI sequence or CT imaging to define the voxels associated with a demarcated “lesion” reconstructed onto templates and mapped to a standardized brain (Dronkers et al. 2004). VSLM methods are best suited for truly focal lesions, but as is now known, there are many disorders – including vascular with a solitary focal lesion – that often have other more subtle abnormalities, which would be missed with the VSLM approach. Even with these limitations, approaches like VSLM have enriched our understanding of how focal pathology relates to various traditional neuropsychological tests (Glascher et al. 2009, 2012; Robinson et al. 2014; Vandenberghe and Gillebert 2009).

See Also

- [Neuroimaging](#)
- [Quantitative Neuroimaging Analysis](#)
- [Voxel-Based Morphometry](#)

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Lethargy

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Synonyms

Apathy; Fatigue

Definition

From the Greek *lēthargia* (from *lēthargos*: “forgetful”), “lethargy” is a general term that can be used to describe either a physical or mental state. Physically, it describes a condition of low energy, which can range from moderate fatigue to severe stupor. When used to describe a mental state, “lethargy” refers to mental inactivity, either from mental fatigue or apathy. Given the range of meanings, “lethargy” does not imply any cause and can be used to describe the malaise of major depression, the muscular weakness of multiple sclerosis, cancer-related fatigue, or the torpor of a nearly comatose state.

Cross-References

► [Stupor](#)

Leukemia

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Short Description

Leukemia is a cancer of the bone marrow, the spongy center of the bones that makes blood cells. It is characterized by the abnormal proliferation of leukocytes (white blood cells). The abnormal white blood cells are not mature and, therefore, cannot carry out their infection-fighting function in the blood. These cells crowd out healthy white blood cells, as well as the red blood cells which carry oxygen to the body and the platelets which cause the blood to clot. Leukemia is part of the broad group of diseases called hematological neoplasms.

Categorization

A fourfold typology classifies leukemia on the bases of the disease's duration from onset to death and of its dominant cell-type (Pui 2003). Acute leukemia is characterized by the rapid generation of immature blood cells (blast cells), which crowd the bone marrow, preventing it from producing healthy mature blood cells. The rapid accumulation of the blast cells can spill over into the bloodstream and spread to organs of the body. In chronic leukemia, there is a gradual build-up of blast cells residing alongside functional cells. With regard to cell type, the disease is classified as *lymphocytic* (or lymphoblastic)

leukemia, referring to abnormal proliferation and cellular development of lymphocytes, or as *myelogenous* (or myeloid) leukemia, referring again to abnormal proliferation and development of granulocytes. Lymphocytes and granulocytes have a primary role in fighting infection.

Epidemiology

In general, acute leukemias are most prevalent in children and are, therefore, often referred to as “childhood leukemias” (Pui 2003). Leukemia comprises almost 25% of all childhood cancers for children <15 years old and peaks between 2–7 years of age (van der Plas et al. 2015). The most common type of childhood leukemia is acute lymphoblastic leukemia (ALL), with an incidence rate of 2.9 per 100,000. Acute myeloid leukemia (AML) is less common, with an incidence rate of 0.52 per 100,000. The chronic forms of these leukemias (chronic lymphoblastic leukemia, CLL and chronic myeloid leukemia, CML) are seen almost solely in adults. The incidence of chronic lymphocytic leukemia in adults is 3.53 per 100,000 and is 1.6 per 100,000 for chronic myeloid leukemia.

Natural History, Prognostic Factors, Outcomes

The causes of leukemia are unknown. Suspected risk factors include exposure to high-energy radiation, some genetic syndromes (including Down’s syndrome), and occupational hazards involving exposure to certain solvents or to electromagnetic fields. Although leukemia is the most common cancer of childhood and the number one cause of cancer-related deaths in children, improvement in its treatment has resulted in high cure rates, particularly for ALL. The 5-year survival rate for children diagnosed with leukemia, and subsequently treated, is now approximately 70%. However, successful therapy has come with a price, as significant morbidity can result from neurological effects of treatments which harm the brain and spinal

cord. This is of specific concern with regard to children who have a particular vulnerability due to their incomplete development and the prospects that their developmental course will be altered by aversive side effects of treatment (Moleski 2000).

Evaluation

For an individual patient, the impressive statistic of an expected 70% 5-year survival rate must be tempered by an evaluation of factors which can better account for expected outcomes in a given situation. Relevant factors include the white blood cell count at diagnosis; case-specific morphological, immunological, and genetic information; a patient’s response to initial treatment; the presence of a genetic disorder, such as Down’s syndrome; and indication of the cancer’s spread to the brain or spinal cord. Potentially important predictive factors also include sex, ethnicity, and age (Moleski 2000).

Treatment

Treatment for acute leukemia can include chemotherapy, steroids, radiation therapy, and intensive combined treatments, including bone marrow or stem cell transplants. Since ALL cells sometimes penetrate the central nervous system (CNS), most protocols include delivery of chemotherapy into the CNS fluid. Whole brain radiation is used for central nervous system prophylaxis to prevent the recurrence of leukemia in the brain. Recent studies showed that CNS chemotherapy produced equally favorable results but with fewer developmental side effects than radiation. As a result, the use of whole brain radiation has been limited. Nonetheless, contemporary treatment approaches which favor the use of chemotherapy (including intrathecal therapy) over radiotherapy in the treatment of ALL can still produce morbid neurotoxicity. Standard neuroimaging is sufficient to identify a variety of neurotoxic sequelae and often suggests a specific etiology. Specific neuroimaging findings frequently indicate a need to alter antileukemia therapy (Pui 2003).

Aside from treatment methods that can worsen side effects, mediation of late effects are proposed through the use of rehabilitative strategies including cognitive training, continuation of academic instruction and presence in school, and pharmacotherapy for cognition and motivation. Learning difficulties that affect school performance and self-esteem, and that may even lead to such problems as chronic unemployment, frequently attend survival following antileukemia treatment. Deficits in fine motor skills, visual-spatial abilities, verbal and nonverbal memory, psychomotor speed, attention regulation, auditory perception, word fluency, and the ability to follow directions have all been reported (Butler and Copeland 2002). The extent of their prevalence has modified the concept of “cure” to include the incorporation of pharmacological and behavioral interventions to optimize the quality of life among cancer survivors (Bearison and Mulhern 1994) as well as their caretakers (Best et al. 2001).

Advances in treatment of cancers involve matching of the genetic characteristics of different cancer types with the pharmacokinetics of treatments. One complication of this is that improved survival is accompanied by increased delayed mental illness and treatment-related psychiatric morbidities. However, a recent Canadian paper suggests that individual human genetic variants may be involved in differences in cognitive outcomes following one known neuropathological treatment – methotrexate. The possible interactions of treatment-induced pathology with cognitive outcomes are reviewed and suggest that treatment could be tailored to the patient’s genotype to minimize adverse effects (van der Plas et al. 2015).

Cross-References

- [Acute Lymphoblastic Leukemia](#)
- [Acute Myelogenous Leukemia](#)

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Leukoaraiosis

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Synonyms

Periventricular leukoencephalopathy (PVL); Small vessel disease; White matter disease; White matter hyperintensity (WMH)

Definition

Leukoaraiosis is a radiological diagnosis referring to rarefaction of white matter and describes brain pathology characterized by diffuse, confluent white matter abnormalities, typically in the

periventricular regions of the brain. Most associated with disease of the small vessels, leukoaraiosis is thought to reflect chronic low-level ischemia in combination with blood-brain barrier dysfunction. Additionally, it may be associated with blood vessel abnormalities, other ischemic events, edema, and cerebral amyloid angiopathy. The underlying pathology includes myelin pallor, enlargement of perivascular spaces, gliosis, axonal loss, and ischemic demyelination. Vascular risk factors, such as hypertension, heart disease, or diabetes, and increasing age are risk factors for developing leukoaraiosis. Leukoaraiosis is detectable by high-frequency CT and MRI and is distinct from other white matter abnormalities, such as lacunes and multiple sclerosis plaques. Symptoms tend to emerge slowly, and the clinical presentation often includes deterioration of gait, depressive symptoms, and cognitive decline. The most prominent cognitive features include reduced processing speed, attentional deficits, and executive dysfunction. Leukoaraiosis has been shown to be a predictor of stroke, falls, dementia, and treatment-related cerebral hemorrhage and is considered a risk factor for death.

Cross-References

- [Binswanger's Disease](#)
- [Gliosis](#)

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Leukodystrophy

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School of Medicine, Braintree, MA, USA

Synonyms

Leukoencephalopathy

Definition

A disorder that causes progressive degeneration of the *white matter* of the brain, a result of abnormal development of or decomposition of the myelin sheath.

Current Knowledge

There are a number of disorders that cause leukodystrophy and each is caused by defective genes that regulate the production or metabolism of one or more components of myelin. Examples of leukodystrophies include *adrenoleukodystrophy*, *metachromatic leukodystrophy*, *Krabbe's disease*, *Pelizaeus-Merzbacher disease*, *Canavan disease*, *Alexander disease*, and *Refsum's disease*. Additional leukodystrophy syndromes with specific genetic abnormalities have recently been described (Schiffmann and van der Knaap 2004). Leukodystrophies are usually inherited but may occur spontaneously as a result of a gene mutation. Inheritance can be autosomal dominant, recessive, or X-linked, depending on the specific disorder. Onset is usually in infancy or childhood and the leukodystrophies typically cause progressive decline in motor and intellectual function. Onset may also occur in adulthood (Sedel et al. 2008). There may be abnormalities in tone, motor strength, coordination, gait, speech, swallowing, vision, hearing, and behavior. Mental and physical development may be slowed, and the disorders may lead to early death. Symptoms vary depending on the particular type of leukodystrophy. The specific genotype helps determine the distinct phenotype, such as behavioral versus motor dysfunction, even within the same disorder, such as metachromatic leukodystrophy (Rauschka et al. 2006). Diagnosis

is made using information from clinical, biochemical, molecular genetics, and MRI evaluations (Phelan et al. 2008; Vanderver 2005).

Cross-References

- [Myelin](#)
- [White Matter](#)

References and Readings

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Leukotomy

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Synonyms

Frontal lobotomy; Leucotomy; Prefrontal lobotomy

Definition

Leukotomy refers to a procedure that involves the interruption of nerve tracts to and from the frontal lobe. It was first introduced in the 1930s by a Portuguese neurologist, Egas Moniz. His original surgery attempted to destroy the fiber tracts connecting the frontal lobe with the rest of the brain via the injection of alcohol. In 1936, he outlined the procedure for the standard “leucotomy.” This procedure was further refined by future neurologists and neurosurgeons and used in the treatment of a number of psychiatric disorders. The procedure led to marked cognitive and personality changes and eventually fell out of favor although more innovative psychosurgical procedures are being considered.

Cross-References

- [Frontal Lobotomy](#)

References and Readings

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Levetiracetam

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Generic Name

Levetiracetam

Brand Name

Keppra XR, Spritam

Class

Anticonvulsant

Proposed Mechanism(s) of Action

Binds to synaptic vesicle protein SV2A and inhibits the activity of negative modulator of GABA and glycine-gated channels; it inhibits N-type calcium current within the neuron.

Indication

Adjunct treatment of partial seizures.

Off-Label Use

Neuropathic pain/chronic pain; mania.

Side Effects

Asthenia, headache, infection, increased blood pressure, drowsiness, fatigue, anorexia, weakness, and nasopharyngitis.

Serious

Suicidal ideation (rare).

Common

Sedation, dizziness, ataxia, asthenia, decreased red blood cell/hemoglobin count, agitation.

References and Readings

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Additional Information

- Drug Interaction Effects. http://www.drugs.com/drug_interactions.html.
- Drug Molecule Images. <http://www.worldofmolecules.com/drugs/>.
- Free Drug Online and PDA Software. www.epocrates.com.
- Gene-Based Estimate of Drug interactions. <http://mhcdaytondes.com:8080/cgi-bin/ddiD4?ver=4&task=getDrugList>.
- Pill Identification. http://www.drugs.com/pill_identification.html.

Levodopa

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Definition

Levodopa or L-DOPA (L-3,4-dihydroxyphenylalanine) is a catecholamine and a precursor of the neurotransmitter dopamine. Neurologic conditions, such as Parkinson's disease (PD), are often associated with low levels of dopamine. As such levodopa therapy is commonly used to treat PD. Upon crossing the blood-brain barrier, levodopa is converted to dopamine. Increasing brain concentration of dopamine can improve the extrapyramidal syndrome associated with PD. Levodopa is marketed under several brand names including Sinemet. In clinical practice, a number of side effects can occur with levodopa therapy including hallucinations and delusions (Ropper and Samuels 2009).

Cross-References

- [Parkinson's Disease](#)

References and Readings

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Lewy Bodies

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Synonyms

Alpha-synuclein inclusions

Definition

Lewy bodies (LBs) are an abnormal aggregation of protein that develops inside the cytoplasm of neuronal cells. LBs contain ubiquitin, alpha-synuclein, and other associated enzymes (see section “[Cell Biology](#)” below for more detail) (McKeith 2000). LBs can vary in size from 8 μm to 30 μm in diameter. There may be a single LB or multiple LBs in a particular neuron (Masterman and Swanberg 2003). They are identified microscopically using histologic staining techniques and typically appear as spherical masses that have a dense core with a surrounding halo (see Fig. 1).

It is generally believed that there are three types of LBs based on anatomic distribution and severity: (1) classical or brainstem LBs, (2) limbic

LBs, and (3) diffuse cortical LBs (McKeith et al. 2005). Recent work has also proposed the addition of an amygdala-predominant subtype that is distinct from the limbic category, but future research is essential to help determine the clinical significance of these categories. Brainstem LBs are easy to see microscopically using conventional hematoxylin and eosin staining, but limbic and cortical LBs can be more difficult to detect since they may lack the characteristic core and halo appearance. Immunohistochemical staining for alpha-synuclein, one of the components of LBs, has emerged as the most sensitive and specific method that is currently available for detecting LBs (McKeith et al. 1996). LB pathology is commonly associated with Parkinson’s disease and dementia with Lewy bodies (DLB).

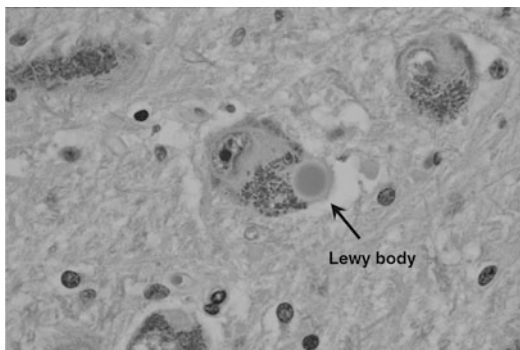
Current Knowledge

History

LBs were first described in 1912 by Friedrich Lewy, a German neuropathologist, who was studying Parkinson’s disease. LB pathology was later linked to dementia, but it was not until the late 1980s, with the development of antiubiquitin immunohistochemical staining methods, that LBs began to be recognized as much more common than previously suspected. Recent studies have suggested that DLB may be the second most common form of degenerative dementia in the elderly, and LBs are a very common neuropathologic finding at autopsy in patients with dementia (Goldmann Gross et al. 2008).

Cell Biology

LBs are believed to be the result of neuronal degeneration that causes a change in neurofilament metabolism and transport, leading to an accumulation of altered cytoskeletal proteins (Masterman and Swanberg 2003). It has been suggested that LBs are not formed at random but instead are produced as an active and regulated process that attempts to control excess amounts of unwanted proteins. Recent immunohistochemical techniques have helped to decipher the molecular composition of LBs, which are now known to



Lewy Bodies, Fig. 1 Lewy body inclusion in the substantia nigra (Image courtesy of James B. Leverenz, M.D. Cleveland Clinic Lou Ruvo Center for Brain Health)

contain a heterogeneous mixture of more than 90 molecules (including a variety of proteins such as neurofilaments, alpha-synuclein, the alpha-synuclein-binding protein synphilin-1, and torsinA), and pale bodies are thought to be the precursors of LBs, containing the material from which LBs develop (Wakabayashi et al. 2013). The granular material in the center of LBs is believed to be made up of ubiquitinated proteins, while the radiating filaments of the periphery consist of alpha-synuclein and neurofilaments. LBs also contain heat shock proteins that play a role in the folding, transport, and degradation of proteins. Although LBs contain many different proteins, there are some proteins that are abundantly expressed in neurons that are *not* typically found in LB inclusions; these include synaptophysin, β -synuclein, γ -synuclein, and tau. LBs also contain lipids but do not have carbohydrates or nucleic acids.

Associated Diseases

The presence of LBs is considered part of the diagnostic criteria for idiopathic Parkinson's disease (PD) and dementia with Lewy bodies (DLB). However, LBs are also present in other neurodegenerative disorders including Hallervorden-Spatz disease, neuroaxonal dystrophy, ataxia-telangiectasia, subacute sclerosing panencephalitis, spinocerebellar degeneration, progressive supranuclear palsy, multiple system atrophy, cortical-basal ganglionic degeneration, and Alzheimer's disease (Alvord and Forno 1992).

Cross-References

- [Dementia with Lewy Bodies](#)
- [Parkinson's Dementia](#)
- [Parkinson's Disease](#)

References and Readings

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Lexicon

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Synonyms

Vocabulary

Definition

The term “lexicon” is sometimes used synonymously with “dictionary.” In the most general sense, a lexicon is a list of lexical units of a language. Characteristics of each unit, such as grammatical class (e.g., noun, verb) and meaning, are typically included in the lexicon. The term “mental lexicon” is used to refer to not only the lexical units stored in an individual speaker/listener's brain but also to the knowledge of the processes and rules by

which the units are manipulated. The mental lexicon is fluid and flexible, changing with the speaker's experience and needs.

Cross-References

► [Semantic Memory](#)

References and Readings

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Lezak, Muriel, Fig. 1

Lezak, Muriel

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Name and Degrees

Muriel Deutsch Lezak, Ph.D., received a Bachelor of Philosophy (Ph.B.) degree in General Studies (1947) and her Ars Magister (A.M.) in Human Development (1949) from the University of Chicago. She was awarded a Ph.D. in Clinical Psychology from the University of Portland, Portland, Oregon (1960) (Fig. 1).

Major Appointments

- Professor Emerita, Neurology; Oregon Health & Science University, Portland, Oregon; 2006–Present
- Professor of Neurology, Neurosurgery, and Psychiatry, Oregon Health & Science University, Portland, Oregon; 1992–2005
- Associate Professor of Neurology, Psychiatry, & Neurosurgery, Oregon Health & Science University, Portland, Oregon; 1985–1991

- Assistant Professor of Neurology, Psychiatry, & Neurosurgery, Oregon Health & Science University, Portland, Oregon; 1979–1985
- Professor of Psychology, University of Oregon, Eugene, Oregon; 1980–1982, 1986–1992
- Faculty Member, American Academy of Judicial Education, Washington, DC; 1974–1978
- Clinical Neuropsychologist, Veterans Administration Hospital, Portland, Oregon; 1966–1985
- Unaffiliated Private Practice, Portland, Oregon; 1966–1985, 2006–Present
- Lecturer in Psychology, University of Portland, Portland, Oregon; 1963–1966
- Counselor, Assistant Professor of Educational Psychology, Portland State College (now Portland State University), Portland, Oregon; 1961–1963
- Chief Psychologist, Clackamas County Child Guidance Clinic, Oregon City, Oregon; 1959–1961
- Staff Psychologist, Community Child Guidance Clinic, Portland, Oregon; 1949–1953

Major Honors and Awards

- Pfizer Travelling Fellow of the Clinical Research Institute of Montreal; September, 1981

- American Psychological Association: Fellow, Division 40 (Neuropsychology), 1983
- Department of Rehabilitation Medicine, Medical College of Virginia, Virginia Commonwealth University: Annual Award for Outstanding Service to the Brain-Injured; June, 1985
- West China University of Medical Sciences (Chengdu, Sichuan Province): Honorary Visiting Professor, 1987
- National Head Injury Foundation: Clinical Service Award, 1989
- Who's Who in Sciences and Engineering, Second Edition, Third Edition, Fourth Edition
- National Academy of Neuropsychology: Distinguished Neuropsychologist, 1996
- American Psychological Foundation: Arthur Benton Lecture; August 6, 2000
- International Neuropsychological Society: Distinguished Career Award, 2008
- University of Chicago: Professional Achievement Award, 2012
- Oregon Brain Injury Alliance: Lifetime Achievement Award, 2013

Landmark Clinical, Scientific, and Professional Contributions

- Dr. Lezak is the author of *Neuropsychological Assessment*, first published in 1976 and now in its fifth edition (Lezak, Howieson, Bigler, & Tranel [2012], NY: Oxford University Press). Each successive edition of Lezak's book has been considered a landmark publication. She edited *Assessment of the Behavioural Consequences of Head Trauma* (1989), NY: Alan R. Liss, and was book review editor of the *Journal of the International Neuropsychological Society* from 1995 through 2004. Dr. Lezak has written many journal articles on neuropsychological assessment issues, the social and family impact of brain disorders, and related topics. She was the first to use the term "executive functions." She is a Diplomate of the American Board of Professional

Psychology in Clinical Psychology and Clinical Neuropsychology, a Fellow of the American Psychological Association (Division 40), and a past president of the International Neuropsychological Society.

Short Biography

Dr. Muriel Deutsch Lezak was born and raised in the Hyde Park neighborhood of Chicago, Illinois. Her father worked as a wholesale furrier, and her mother was a homemaker. She met her husband, Sidney Lezak, when she was only 8 years old and he was 11, and his family became apartment building neighbors. They began dating in May 1946 while both attended the University of Chicago. They married in June 1949 and moved to Portland, Oregon, that day. Their marriage and careers flourished. Sidney Lezak served as U.S. Attorney for the Federal District of Oregon for 21 years, and Dr. Lezak began her groundbreaking work in neuropsychology. She and her husband had three children, David, Anne, and Miriam, and nine grandchildren. They were married for 56 years before he died in April 2006. She enjoys traveling, playing piano, going to the theater and movies, and spending time with friends and family.

Dr. Lezak obtained a doctorate in Clinical Psychology from the University of Portland in 1960. She was a counselor at Portland State University and in private practice until 1966. She joined the staff of the Veterans Administration (VA) Medical Center in Portland, Oregon, in 1966 where she had an intensive experience working with patients with brain injury on both the acute wards and in rehabilitation. Her work with these individuals led to VA-funded research on their cognitive problems. This evolved into a study of emotional/psychosocial consequences of traumatic brain injury for which she developed the precursor of the *Mayo-Portland Adaptability Inventory*. While employed at the VA, she also became an assistant professor of Neurology at Oregon

Health and Sciences University. In 1985, she moved to a full-time position at Oregon Health and Science University, becoming Professor Emerita (Neurology) in 2006. She also maintains a private practice in neuropsychological consultation.

In addition to her significant professional contributions to the fields of neuropsychology, clinical psychology, neurology, and psychiatry, Dr. Lezak also devoted a significant amount of time to public service. She served on numerous councils, advisory boards, and committees for the American Psychological Association (APA), Family Survival Project for Brain Damaged Adults, the National Institute of Health Coma Data Bank Project, American Association of State Psychology Boards, Oregon Head Injury Foundation, the California State Athletic Commission, National Institute of Aging, Oregon State Bar/Oregon Supreme Court, and the Institute of Medicine of the National Academies to name only a few.

Cross-References

- ▶ [American Academy of Clinical Neuropsychology \(AACN\)](#)
- ▶ [American Board of Clinical Neuropsychology \(ABCN\)](#)
- ▶ [American Board of Professional Psychology \(ABPP\)](#)
- ▶ [American Psychological Association \(APA\), Division 40](#)
- ▶ [International Neuropsychological Society](#)
- ▶ [Mayo-Portland Adaptability Inventory](#)

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Liepmann, Hugo Karl (1863–1925)

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Major Appointments

- Assistant to Wernicke (Breslau, Germany, 1895–1899)
- Municipal Welfare for the Mentally Ill in Berlin
- Assistant and Consultant for Psychiatric Hospital of Dalldorf
- Director of Psychiatric Hospital in Herzberge (1914–1920)
- Private Lecturer (University of Berlin, 1901–1905)
- Professor (University of Berlin, 1905–1919)
- Honorary Professor and Secret Medical Counselor (University of Berlin, 1919)

Major Honors and Awards

- President of the Berlin Society for Psychiatry and Nervous Diseases (1912–1916)

Landmark Clinical, Scientific, and Professional Contributions

- The German neurologist and psychiatrist Hugo Karl Liepmann is best known for his work on apraxia. Although John Hughlings Jackson was the first to clearly define the syndrome of apraxia in 1861, he did not fully elucidate the concept. Liepmann coined the term “apraxia,” delineated associational cortical areas, and distinguished among three types of apraxia: (1) limb-kinetic (melokinetic), (2) ideomotor, and (3) ideational (Heilman et al. 2003). He proposed that apraxia was clearly a disorder of motor planning (Rothi and Heilman 1996).

From extensive anatomical studies, Liepmann contributed to the field's knowledge of cerebral localization of function. As such, he claimed that motor plans were localized to the parietal lobe rather than the frontal lobe.

- In his seminal paper on apraxia highlighting the case of “Mr. T” in 1900, Liepmann refined the term apraxia to include disorders of purposeful movement exclusive of primary motor dysfunction, asymbolia, and object recognition deficits. As such, his definition suggested that purposeful movement can be localized to a specific brain region that is consequently susceptible to circumscribed impairment (Rothi and Heilman 1996). Between 1900 and 1905, Liepmann extended his research from a single case study to examining 83 patients' performance of imitation, pantomime, gesture, and actual object use (Rothi and Heilman 1996). He had a particular interest in the role of the right and left cerebral hemispheres in motor planning. In his 1905 paper, he hypothesized that a specialized system devoted to motor programming exists in the left cerebral hemisphere. He also delineated specific components of such a system, which included “(1) the movement formula, (2) the ability to realize a movement's innervations, and (3) kinetic memories for overlearned movements” (Rothi and Heilman 1996). Expanding upon his observations, Liepmann delineated several apraxia syndromes including motor apraxia, innervatory apraxia, ideational apraxia, and callosal apraxia. Overall, Liepmann's comprehensive investigations into apraxia were some of the most innovative concepts of his time, particularly with his claim that disorders of skilled motor planning are not accounted for by object agnosia or asymbolia. Furthermore, his suggestion that clinicians could discover underlying mechanisms that lead to limb apraxia via clinical testing and error response assessment was truly remarkable for his time.

Short Biography

On April 9, 1863, Hugo Karl Liepmann was born into a wealthy Jewish family in Berlin, Germany.

His family instilled in him an intellectual curiosity that crossed over various cultural lines. During his school years, he cultivated his interests in philosophy and ancient languages, studying Greek and German literature. His quest for knowledge continued throughout university where he voraciously read philosophy, linguistics, chemistry, and psychology. From 1880 until 1885 when he obtained his Ph.D., he studied the natural sciences in Leipzig, Freiburg, and Berlin. His Ph.D. thesis was based on the mechanism of Leukipp-Democrit's atoms, founded upon the philosophy of ancient Greece (Goldenberg 2003; Liepmann and Hamburger-Liepmann 1977). Kant and Schopenhauer emerged as most influential in Liepmann's life. However, over time, philosophy no longer satiated his appetite for learning, and he yearned for the exactness of medical science. Thus, he began reading medical literature in his late twenties, passed his final medical examination in 1884 in Berlin, and obtained his M.D. in 1895.

Reflecting on their father's youth and early life, his daughters noted that Liepmann enjoyed hiking, traveling, and savoring delicacies in the company of friends (Liepmann and Hamburger-Liepmann 1977). They further described how Liepmann periodically experienced self-doubt and sadness throughout his early years and into adulthood. For a few years after meeting his wife-to-be, Liepmann experienced more moments of happiness and joy. During their early childhood, Liepmann's daughters viewed him as a true “absent-minded professor” who periodically locked family members in his office by mistake when he quickly ran off to see patients on the wards. From 1885 to 1886, Liepmann served as a horse guard in the German Army. Thereafter, his love of horses remained. He frequently rode his horse from house to house within the Herzberg hospital (Goldenberg 2003). Liepmann's daughters further described their father as having high integrity and a true sense of justice coupled with a keen sense of humor.

Soon after he graduated with his M.D., Liepmann worked under the tutelage of Wernicke in Breslau where he remained until 1899. Liepmann then returned to Berlin where he accepted a position at the municipal welfare for the mentally ill (Goldenberg 2003). He also held positions as assistant and consultant in the Dalldorf

psychiatric hospital. After his 15-year tenure at Dalldorf ended in 1915, he assumed the position as director of a large mental institute at Herzberge where he remained until 1920. With regard to his university affiliations, Liepmann became private lecturer at the University of Berlin in 1901 and was appointed professor in 1905. In 1919, he earned the title of honorary professor and secret medical counselor. His children asserted that he was never awarded an academic chair position because of his Jewish faith (Liepmann and Hamburger-Liepmann 1977). They recount one incident during which he was offered a chair position and would have been awarded the position had he renounced Judaism. Liepmann's daughters also acknowledged that he suffered extreme stage fright with regard to giving lectures. He was frequently worried about boring his audience, even though he was described as an excellent and popular lecturer.

Liepmann was described as a man of high ethical standards both in his professional and personal lives. His family donated one of their homes to the Israelitic Educational Institute and Children's Sanatorium. Additionally, during World War I, the Liepmanns hosted a different welfare institution in their second home (Lammel 1993).

Liepmann continued his involvement in the Berlin Society for Psychiatry and Nervous Diseases into his later years. He had served as president of the society from 1912 to 1916. He resigned from his position at Herzberge due to progressive Parkinson's disease. He was astutely aware of his declining neurocognitive abilities and on May 6, 1925, at age 62 committed suicide. Liepmann will be remembered for his integrity of character, strong commitment to fairness, and significant contributions to the field of neurology and neuropsychology.

Cross-References

► Apraxia

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Life Care Planning

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Definition

The life care planning (LCP) process uses a systematic methodology to identify and quantify the multidimensional disability-related needs of an individual who has experienced catastrophic injury or who needs significant disability-related

services throughout his or her life. The results of this process are summarized in a life care plan, which has been defined as “a dynamic document based on published standards of practice, comprehensive assessment, data analysis, and research, which provides an organized concise plan for current and future needs with associated costs, for individuals who have experienced catastrophic injury or have chronic health care needs (Weed and Berens 2010).” The purpose of a life care plan is to serve as a “road map” to inform the person with a disability, her or his family members, and service providers about anticipated disability-related needs and services necessary (at which points in time) to meet those needs. The goal of the LCP process is to design a recommended set of services that will maximize function and quality of life for the person with a disability while minimizing overall costs. Proactive prevention of complications, minimizing reactive responses to chaotic crises, is a hallmark of LCP practice. The life care plan should address not only medical needs but psychological, vocational, educational, social, and independent living needs as well.

The process of LCP uses a consistent transdisciplinary methodology for gathering disability-related information about an individual, integrating that information, requesting additional information (e.g., from the individual with a disability, family members, and current treatment providers), reviewing relevant research literature, developing recommendations for services, researching availability and costs of such services in the individual’s local area, and synthesizing this information into one comprehensive document. The life care plan document itself is usually presented in the form of a narrative summary followed by a set of tables, with each page of the tables focusing on a different dimension of disability-related needs and services. Examples of categories for those pages include projected health-related professional evaluations, projected therapeutic modalities, diagnostic testing and educational assessments, wheelchair requirements, wheelchair accessories and maintenance, orthopedic equipment needs, orthotics or prosthetic needs, disability-related home furnishings and accessories, aids for independent function, drug

and supply needs, home care or facility-based care needs, projected routine future medical care, projected future surgical treatment or other aggressive medical care, health and strength maintenance (recreation) needs, and vocational services needed. These categories are presented separately for two main reasons: (1) they help consumers, family members, and service providers to understand the many areas of attention needed to prevent complications and maximize quality of life, and (2) they tend to be associated with different growth rates for projected costs, facilitating analysis by an economist or financial planner. Within each category, the specific services recommended are identified, along with the projected dates and frequencies needed, with a range of costs for those services. Following the tables of specific services and their costs is a list of potential complications, for educational purposes. Complications are possible problems with a low or unknown probability of occurring. If something is “more likely than not” to occur for the given individual despite proactive preventative services, it is considered a projected need, rather than a complication; it is then detailed in the life care plan recommendations.

Cross-References

- ▶ Case Management
- ▶ Disability
- ▶ Discharge Planning
- ▶ Forensic Neuropsychology
- ▶ Rehabilitation Counseling
- ▶ Rehabilitation Psychology

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Lighthouse Technique

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Synonyms

Mental Imagery

The Lighthouse Technique (LHS) combines mental imagery and attention training and was developed (Niemeier 1998) to address the devastating effect of neglect on long-term post-injury recovery and outcomes (Heilman et al. 1997). Inclusion of the component of mental imagery was informed by the sports psychology literature on performance enhancement (Williams and Leffingwell 1996). The LHS is also based on the cognitive rehabilitation research findings, supporting the effectiveness of attention and memory training (Cicerone et al. 2005; Luukkainen-Markkula et al. 2009; Marshall 2009; Sohlberg and Mateer 2001; Wilson 1987) for persons with brain injury. Since the development and testing of the Lighthouse Strategy, investigators and reviewers have repeatedly cited it as a unique and effective, evidence-based mental or visual imagery strategy for reinforcing patient's direction of attention following brain injury (Bailey et al. 2002; Bryck and Fisher 2012; Maxton et al. 2013; Welfringer et al. 2011) and application for adults and children. It stands as the only

intervention of its kind in systematic reviews of literature on rehabilitation of unilateral neglect (Cicerone et al. 2005; Luaute et al. 2006; Riggs et al. 2007). The Lighthouse Strategy is featured in biannual training in cognitive rehabilitation by the American Congress of Rehabilitation Medicine and is published in their Cognitive Rehabilitation Manual (Haskins et al. 2012).

Definition

The Lighthouse Strategy (LHS) is both an evidence-based (Cicerone et al. 2005; Heilman et al. 1997; Niemeier 1998, 2002; Niemeier et al. 2001) cognitive rehabilitation intervention and compensatory strategy for improvement of left or right hemispatial inattention following brain injury. The goal of the LHS is to train persons with brain-injury-related neglect to self-manage and prevent unsafe behaviors commonly exhibited with this deficit.

Current Knowledge

Pretreatment assessment is completed using the Mesulam Verbal Cancellation Test (MVCT) (Mesulam 2000), the Cross Drawing (CD) task from the Reitan-Indiana Aphasia Screening Test tasks of the Halstead-Reitan Neuropsychological Test Battery (Reitan and Wolfson 1993), and review of the patient's Functional Independence Measure (FIM™) (Hall et al. 1996) scores. Therapists then conduct three, 30-min training sessions.

Training Session One Therapists position patients in the middle of a long, uncluttered table. A simple line drawing of a lighthouse (Niemeier 1998) is used to make an analogy between consequences for ships and persons who are not able to see where they are going. This introduction paves the way for demonstration of how patients can become like lighthouses to improve their own safety. With demonstration of how to move head and eyes together and the level of cuing needed, therapists ask patients to find first three-dimensional objects and then flat

pictures of objects placed in front of them. All other therapists are informed that patients have begun LHS training and the level of cuing they require.

Training Session Two Therapists review the LHS and go back over the picture again at the beginning of the session. Patients are then taken around the environment and are asked to point out objects on the left or right side. Cues to use the LHS are given when needed.

Training Session Three After the opening review, therapists provide patients with a route-finding task with instructions to avoid bumping into anything. If patients are not able to propel their wheelchairs, therapists serve as drivers and ask patients to be navigators, telling therapists which way to turn. Cues are given as needed.

Patients are reassessed with the MVCT, CD, and FIM scores after session three.

Additional Clinical Uses In addition to LHS steps already described, there are several other possible therapeutic components of the LHS. The provision of a visual image may help patients avoid the cognitive fatigue involved in having to recall an image. To enhance carryover, all therapists on patients' rehabilitation teams use the same image and LHS cues. The scope of the LHS training tasks are graduated and task relevance to real-life functioning is increased over the three training sessions.

Limitations of the method include lack of randomization of the effectiveness trials, the level of abstraction required for grasping the lighthouse-human metaphor, no long-term follow-up in controlled trials, and exclusion of patients with global aphasia.

Since the development and testing of the Lighthouse Strategy, investigators and reviewers have continued to cite it as a unique and effective, evidence-based mental or visual imagery strategy for reinforcing patient's direction of attention following brain injury (Bailey et al. 2002; Maxton et al. 2013; Welfringer et al. 2011). It stands as the only intervention of its kind in systematic reviews of literature on rehabilitation of unilateral neglect

(Riggs et al. 2007). In addition to use in improving hemispatial inattention, more recent studies have suggested its use for rehabilitation of BI visual inattention in pediatric populations and cueing use of the LHS during functional tasks such as wheelchair driving.

Cross-References

► Attention Training

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Limbic System

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Synonyms

Limbic lobe

Definition

The “limbic lobe” of the brain is an arcuate convolution of cortex on the medial aspect of the cerebral hemisphere surrounding the corpus callosum and extending into the parahippocampal gyrus of the temporal lobe.

Current Knowledge

The “limbic lobe” of the brain, originally defined by Broca, is an arcuate convolution of cortex on the medial aspect of the cerebral hemisphere surrounding the corpus callosum (subcallosal gyrus and cingulate gyrus) and extending into the parahippocampal gyrus of the temporal lobe. The term “limbic system” includes other subcortical structures that entertain connections with the limbic lobe, and collectively function in various aspects of emotionality. Since “affect” and emotion are an integral part of many human behaviors, these structures are involved in such activities as diverse as memory processing, pleasure/reward, reproductive and feeding behaviors. Some of the principal limbic system structures (in addition to the limbic lobe cortex) include the hippocampal formation, amygdala, hypothalamus, and basal forebrain (e.g., ventral striatum, nucleus accumbens), and the major fiber systems that interconnect them. Lesions of the ventromedial temporal lobe that include the hippocampal formation typically result in anterograde amnesia. The amygdala functions to add emotional salience to sensory experience. Lesions of the amygdala typically result in Kluver-Bucy syndrome, which includes a lack of emotion. The nucleus accumbens in the basal forebrain has been called a “center for addiction” since it is the terminus of the dopaminergic mesolimbic “reward” system, and is activated in pleasurable experiences. Working in concert with the hippocampus, the basal forebrain has also recently been shown to play a critical role in declarative memory (DeLuca et al. 2003).

Cross-References

- [Amygdala](#)
- [Basal Forebrain](#)

- Dopamine
- Hippocampus
- Hypothalamus
- Klüver-Bucy Syndrome

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Line Bisection

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Synonyms

Tests of visual inattention

Description

A simple task wherein the examinee is asked to draw a line that bisects lines of varying length. Diller et al. (1974) presented a technique in which the examiner draws the line for the patient or instructs the patient to copy an already drawn horizontal line. The patient is then asked to divide the line in half by placing an “X” on the center point. Schenkenberg et al. (1980) developed a multiple trial line bisection test that uses a set of 20 lines of varying sizes arranged so that six are centered to the left of the midline on a $8\frac{1}{2} \times 11$ sheet of paper, six to the midline, and six in the center along with a top and bottom line to be used for instructions are centered on the page. The examiner then asks the patient to “cut each line in half by placing a small pencil mark through each line as close to its center as possible.”

Historical Background

Diller et al. (1974) presented a technique using a single line, and Schenkenberg et al. (1980) developed a multiple trial line bisection test; however, the process of examining for unilateral inattention by using a line bisection has been long used.

Psychometric Data

With a single bisection line (Diller et al. 1974), the score is the length by which the patient’s estimated center deviates from the actual center of the line. With the multiple trial lines (Schenkenberg et al. 1980), only the middle 18 lines are scored. Test-retest correlation runs in the 0.84 to the 0.93 range.

Clinical Uses

This test is used to assess unilateral inattention. Often patients with right-sided lesions give greater deviations to the right, and patients with left-sided lesions move the bisection further left (Pasquier et al. 1989). Noticeable errors are often made by patients with visual field deficits (Lezak et al. 2004).

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Lingual Gyrus

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Definition

Gyrus on the medial surface of the occipital lobe, lying just below the calcarine fissure (see figures in “► [Calcarine Fissure](#)” and “► [Cuneus](#)”). It represents part of the primary visual cortex, receives direct input from the ipsilateral lateral geniculate nucleus, and is supplied by the posterior cerebral artery. The visual input to the lingual gyrus ultimately originates from the inferior portion of the retinas (inferior temporal portion of the ipsilateral eye and inferior nasal portion of the contralateral eye). Thus, a lesion involving this gyrus would be expected to result in a contralateral superior homonymous quadrantanopsia.

Cross-References

- [Calcarine Fissure](#)
- [Visual System](#)

Lisdexamfetamine Dimesylate

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Generic Name

Lisdexamfetamine Dimesylate

Brand Name

Vyvanse

Class

ADHD agents; stimulants

Proposed Mechanism(s) of Action

Vyvanse is a prodrug of dextroamphetamine and induces the release of dopamine and norepinephrine from their storage areas in nerve terminals.

Indication

Attention deficit/hyperactivity disorder, binge eating disorders in adults.

Off-Label Use

Treatment resistant depression.

Side Effects

Headache, hypertension, nausea, nervousness, tachycardia, angina, cardiac arrhythmia, anxiety, anger, agitation.

Serious

Psychotic episodes (particularly with IV abuse), seizures, tachycardia, hypertension, rare neuroleptic malignant syndrome, activation of manic episodes, and sudden cardiac death with those with preexisting neurocardiogenic defects.

Common

Insomnia, headache, nervousness, irritability, overstimulation, tremor, dizziness, anorexia, nausea, abdominal pain, weight loss, and blurred vision.

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Additional Information

Drug Interaction Effects. http://www.drugs.com/drug_interactions.html

Drug Molecule Images. <http://www.worldofmolecules.com/drugs/>
 Free Drug Online and PDA Software. www.epocrates.com
 Free Drug Online and PDA Software. www.medscape.com
 Gene-based Estimate of Drug Interactions. <http://mhcd.taytondcs.com:8080/cgi-bin/ddiD4?ver=4&task=getDrugList>
 Pill Identification. http://www.drugs.com/pill_identification.html

Literal Paraphasia

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Synonyms

Fluent segmental paraphasia; Phonemic paraphasia; Phonological substitution

Definition

The Greek prefix “para” means “substitution for” and, when affixed to “-phasia,” came to mean a substitution in speech. “Literal” paraphasia was the term for a substitution of a sound segment developed from early research on aphasia in languages with alphabetic writing systems and before the conceptualization of the “phoneme” at the end of the nineteenth century.

Under many important constraints, one phoneme may substitute for another, and as phonemes are understood as a “set of distinctive features,” there is a metric to evaluate phonemic substitutions in terms of the number of shared features between target and error. A majority of phonemic paraphasias, although not all, involve phonemes that differ in only one feature, and thus one can see that “like substitutes for like”: /p/ → /b/ differing in the feature for voice, /n/ → /m/ differing in the feature for place of articulation, and /t/ → /s/ differing in the feature for manner, from an oral stop

to a fricative, and the like. Most often, it has been observed that the substituted phoneme is somewhere in the nearby context – either previously produced or upcoming. Consequently, linear ordering is often involved in phonemic paraphasia. The smaller a target word is, the more likely that a phonemic paraphasia of it will result in another word, but as the word gets longer, a phonemic paraphasia is more likely to produce a “nonword.” Rarely do phonemic paraphasias result in a word that is not pronounceable by the speaker. Finally, it is a “category mistake” to claim that sounds are substituted for each other. Phonemes are “sets” of sounds; they are *not* sounds, and it is the set that substitutes for another set; sounds are not involved, nor obviously are alphabetic letters.

Historical Background

In modern day parlance, researchers in the language sciences (linguistics, speech pathology, psycholinguistics, phonetics, phonology, neurolinguistics, and linguistic aphasiology) refrain from labeling segmental substitutions as “literal paraphasias.” This is an antiquated definition of the phenomenon, a definition that stretches back to the days before Baudouin de Courtenay (1885–1886) hit upon the concept of the phoneme, after considering the growth of sound types in any one language that were being discovered and described in the burgeoning field of phonetic science in the late nineteenth century. From that point on, language investigators slowly began to appreciate that speakers and hearers are only consciously aware of the segments they produce and hear daily at the level of the phoneme and not at the level of individual articulated sounds. It was clear to scholars like Baudouin that the human language user was incapable of any conscious awareness of the wealth of sounds that were being described by more sophisticated descriptive phonetic science. Rather, what one thinks one is hearing and uttering are phonemes, but what one is hearing and uttering in the physical world are more properly sounds.

It goes without saying that substituting these “abstract” psychological units (Sapir 1921, 1949)

was not and had never been “letter” substitutions. It became ludicrous to consider that humans articulated letters. Early investigators did not have the luxury of the concept of the phoneme, and what made the situation even more confusing was that these early investigators spoke native languages that by chance had alphabetic writing systems, such as German, French, and English, so they inadvertently used the term letter, thus “literal.”

Current Knowledge

Long since the days when the ancient Greeks added vowel letters to the consonantal writing system of the Phoenicians, many who have commented in one way or another on human spoken and written language have conflated “sounds” with “letters,” falling into this trap because most Western languages have either Roman- or Greek-related writing systems – alphabetic systems using graphic segments called letters or more properly called “graphemes.” Not only are sounds not phonemes, the phonemes themselves should not be confused with letters, although scholars in the history of writing have realized that the alphabetic writing systems were crafted from phonemic-level knowledge and not from any direct knowledge of physical sounds. Phonemes and sounds qua sounds do not share the same ontological status, nor do phonemes and letters; their essential natures are distinct. Reading specialists must be acutely aware of these distinctions, as the newly mined field of “phonological awareness” treats the fascinating cognitive interface between letters and phonemes in beginning and pre-readers, not between letters and sounds.

What is known is that letters in the English writing system are quite complex in their relations with English language phonemes, which is not the case in a language such as Spanish. This is why, in the Spanish-speaking world, there is no concept or interest in the “spelling bee.” Letter-phoneme matches are much more direct in the Spanish writing system, except for a very few cases. Languages such as English and French have gone through drastic phonological changes in their spoken forms, with few if any “spelling reforms.”

One must be clever to spell consistently and correctly in these languages – not so for Spanish.

In the end, visual graphemic shapes should not be confused with phonemes, and accordingly, one should consider the term “literal paraphasia” to be an outmoded term. Furthermore, “sound” substitutions turn out to be phoneme substitution in practically every case of a segment switch.

A few examples of phonemic paraphasia will be beneficial to the reader. Ironically enough, the pure substitution of one phoneme for another is rare if there is no contextual source for the error phoneme. Here are some examples for which I could find no contextual source:

1. Lovely → lofely (/v/ → /f/, voiced, labiodental, fricative → voiceless, labiodental, fricative). Typical of the “no source” substitution is that the target and error differ in only one distinctive feature; here the switch involves the feature of voicing, place and manner remaining unchanged. The question here is always whether the substitution was a full set of features for another full set of features or whether the error is best considered to be the change of only one feature.

As it turns out, the great majority of phonemic paraphasias has the error phoneme somewhere fairly near the target:

1. Socially → sosilly (/sh/ → /s/, voiceless, alveopalatal, fricative → voiceless, alveolar, fricative). Here the error involves only one feature, that of place, but note that there is another/s/in the word onset of the target word.

In 2, the source was to the *left* of the error site. Sometimes the source is to the *right* of the error source:

1. Horse → sores (voiceless, glottal, fricative → voiceless, alveolar, fricative). Once again, there is a switch of only one feature; here it is the place of articulation. As opposed to 1 and 2, this error output happens to be a word in English (source). The so-called lexical bias must be noted here, as many full word errors

have been seen in the study of *verbal* paraphasias, where the substitution is among full-fledged words. And it has recently been discovered that these kinds of word substitutions are phonologically very close. Here, the words would be phonological associates and not semantic associates.

At times, phonemic paraphasias will be full reversals, often called exchanges or metathesis:

1. Driving → derving (where the /t/ moves from prevocalic position to postvocalic position) Also, see thirty → threety, although the free morpheme “three” may have substituted for the bound morpheme “thir-.” Often, scholars analyzing phonemic paraphasia are left with an intractable ambiguity. In such cases, it is necessary to further search the errors of the patient to see if there is a pattern of errors one way or the other.

As there are far more consonants than vowels in most languages, most phonemic paraphasias involve consonants; this does not have to be the case:

1. Analyst → aynalyst (where the pure vowel /ae/ is replaced by the diphthong /ay/).

Diphthongs function in phonemic paraphasia for the most part as single phonemes, that is, most analyses of “hit” vs. “height” are that both are words that have a consonant-vowel-consonant pattern (CVC words).

All phonemic paraphasias obey a set of constraints that restricts the structure. First, they are always phonemes of the speaker’s language. Second, the errors that result do not form phonotactic patterns not permitted in the language; “swell” might become “slell” by substitution of the coda /l/ for the /w/, but rarely if ever for the /s/, to give /lwel/. Another important constraint on phonemic paraphasias is that, with the exception of within syllable movement substitutions, the syllable constituency of right-to-left or left-to-right ordering errors remains the same, that is, onsets move to onset positions, vowels

move to vocalic positions, and codas move to coda positions. In English, if the source of the movement is a consonant in “ambisyllabic” position, it can move to either an onset or a coda constituent position. In English, an “ambisyllabic” consonant is a singleton within a two-syllable trochee (strong stress – weak stress), such as the /l/ in “silly” or the /n/ in “funny.” These constraints on phonemic paraphasias are also those observed in the segmental slips-of-the-tongue in neurotypical speakers. There is a rich literature on phonemic paraphasia, much of it covered in Buckingham (1989, 1992) and later works.

Phonemic paraphasias should be evident in the speech of patients who are free of motoric disruptions, that is, phonemic paraphasia is seen mainly in patients with posterior perisylvian cortical disruption, and for CVAs, one expects posterior MCA involvement. These patients most often test out either as having Wernicke’s aphasia of different types or as having conduction aphasia, often with more than simply repetition disabilities. People with severe Wernicke’s aphasia and severe conduction aphasia may both produce complicated nonwords, which many call neologisms. Given that almost all adults with aphasia have word-finding difficulties, those conduction aphasics who also have lexical access problems will produce many phonemic paraphasias. The diagnostic distinction here, of course, is that the person with conduction aphasia tends to understand much better than the person with Wernicke’s aphasia. It has also been observed that many people with conduction aphasia tested out initially as having Wernicke’s aphasia but regained enough comprehension to evolve into a conduction-type patient.

The difficulty with the phonemic paraphasia in the production clutter of a person with Broca’s aphasia with apraxia of speech is that, for any one supposed *phonemic* level error, there is the real possibility that an apraxic speech asynchrony may alter the acoustic spectrum of some intended phoneme, but where the altered acoustic spectrum is such that hearers perceive *another* phonemic unit. The well-known problem with VOT is replete with

phonemic boundary crossover in the speech of adults with apraxia of speech. This serious conundrum for the clinician is further discussed in Buckingham (1989, 1992).

Not only do adults with Wernicke's aphasia recover comprehension at different rates, but such improvement often brings about a new aphasia category for the patient. In this case, the person with Wernicke's aphasia with recovered understanding will often then fit into the symptom complex of conduction aphasia. Throughout recovery of fluent phonemic paraphasic speech, one often sees improved self-monitoring, whereby the patient catches pre-articulatory an error about to occur, and blocks it. Others, with a very severe phonological output problem, will often recover to an isolated word finding. The anomia at the end stage is interpreted as evidence that the anomia was there from the beginning but masked by the large amount of jargon surrogates for inaccessible words in the early stages.

Most therapy protocols for the people with fluent aphasia with phonemic paraphasias are more effective once the patient gains more comprehension and an accompanying control of self-monitoring. At this point, the client is given tasks involving perceiving minimal pair words (some call them cognates) either by repeating or by choosing between two pictures of objects whose words differ in only one distinctive feature, such as a picture of a "pail" and another showing "mail." Engaging the client in other speech response therapies or more work in group therapy often helps them catch errors either pre-articulatory or post-production and subsequently attempt to correct them. It is important to note that for these patients, motor-oriented speech gesturing tasks are not warranted, as people with these types of aphasia should have only very moderate motoric problems at most. Also, this should correlate with little or no right hemiparesis, and the patient should be ambulatory. They should not suffer from apraxia of speech or have oral-facial apraxia. Recovery patterns in patients with phonemic paraphasia have been extensively studied, and more on this can be found in Buckingham (1989, 1992).

Future Directions

Phonemic ordering errors in the direction of right-to-left are called "perseverative" or carry-over, while phonemic ordering errors in the direction of left-to-right are called "anticipatory." Recall the examples above. A fascinating correlation was made a few years ago by Martin and Dell (2004). They first noted that phoneme slips-of-the-tongue are overwhelmingly anticipatory. They then observed that in the severe phonemic paraphasias in early stages of fluent aphasia are perseverative, that is, the phonemes are misordered by carrying them over from left-to-right. Their subsequent study showed that as the patients improve and recover over time, the number of perseverations falls off, compared to the anticipation errors. Martin and Dell developed an "anticipatory/perseverative" (AP) ratio and clearly demonstrated that the AP ratio increases for anticipation errors as the patient improves. This, therefore, is a new way to chart recovery in fluent aphasia, and accords with the findings from slips-of-the-tongue, because the slips are produced by neurotypical speakers. And that is precisely what the recovering adult with aphasia is approximating. More work in the AP ratio and recovery from phonemic paraphasia will be seen in the future.

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Lithium

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Generic Name

Lithium

Brand Name

Eskalith, Eskalith CR, Lithobid, Lithostat, lithium
carbonate, and lithium citrate

Class

Mood stabilizer

Proposed Mechanism(s) of Action

Unknown and complex acts on second messenger
system, modifies sodium transport across cell
membranes (nerve and muscle cells), and mod-
ifies neurotransmitter metabolism (serotonin and
catecholamines)

Indication

Manic episodes and maintenance of manic-
depressive illness

Off-Label Use

Bipolar depression, major depressive disorder,
neutropenia, and headache (vascular)

Side Effects

Leukocytosis, polyuria/polydipsia, dry mouth, hand
tremor, confusion, decreased memory, headache,
muscle weakness, ECG changes, nausea, vomiting,
diarrhea, hyperreflexia, muscle twitch, and vertigo

Serious

Lithium toxicity, renal impairment, nephrogenic
diabetes insipidus, arrhythmia, bradycardia,
hypotension, flattening and inversion of T wave,
pseudotumor cerebri, and seizures

Common

Ataxia, tremor, polyuria, polydipsia, diarrhea,
nausea, weight gain, goiter (euthyroid or hypothy-
roid), acne, alopecia, rash, and leukocytosis

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Additional Information

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Litigation

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Synonyms

Civil action

Definition

Litigation is a lawsuit or a civil action brought before a court in which the plaintiff seeks a legal remedy. One or more defendants are required to respond to the plaintiff's complaint. If the plaintiff wins their case, damages may be awarded. If a lawsuit is not settled by agreement between the parties out of court, it would eventually be heard and decided by a judge or jury in a court. Litigation is one way that people and companies resolve disputes.

Cross-References

- ▶ [Arbitration](#)
- ▶ [Mediation](#)

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Lobar Hemorrhage

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Definition

A lobar hemorrhage occurs when there is bleeding into a lobe of the cerebrum.

Current Knowledge

Because most hemorrhages into the brain occur in the deeper tissues and brain stem, a lobar

hemorrhage is often considered to be a distinct pathogenetic subgroup. It can be caused by a cerebral angioma, aneurysm, or arteriovenous malformation or rarely by sudden acute extreme hypertension, all of which lead to a hemorrhagic stroke; bleeding into a brain tumor; a bleeding disorder, including hemophilia or thrombocytopenia; or trauma. It can also be associated with liver disease, autoimmune disease, and cerebral amyloid angiopathy. At times, no cause can be found. Presenting features reflect those of a hemorrhagic stroke and depend on the location and amount of the brain tissue affected. Symptoms can include altered consciousness and cognition, severe headache or seizure, stiff neck and vomiting, reduced sensation and motor control, swallowing and language difficulties, and others. Increased intracranial pressure causes most of these symptoms. Diagnosis most often relies on cerebral imaging. Treatment may include medications, surgical procedures, or both and at times consists only of observation, symptom management, and rehabilitation. Complications include seizure, hydrocephalus, and persistent neurological deficits. Outcome depends on the amount of swelling and bleeding. Permanent brain damage resulting in disability, or death, may result, and cerebral amyloid angiopathy is characterized by multiple recurrences of lobar hemorrhages.

Cross-References

- ▶ [Angioma, Cavernous Angioma](#)
- ▶ [Cerebral Amyloid Angiopathy](#)
- ▶ [Hemorrhagic Stroke](#)
- ▶ [Intracerebral Hemorrhage](#)
- ▶ [Intracranial Hemorrhage](#)
- ▶ [Vascular Malformations](#)

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Lobectomy

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Definition

A “lobectomy” is a surgical procedure for removing a diseased or damaged portion of a solid tissue such as the lung, liver, or brain. Removal of damaged and/or diseased parts of the brain may be necessary after TBI, neoplasms, intracranial hematomas, and occasionally in cases of severe brain infection. Untreated, such conditions can cause increased intracranial pressure and further damage to nearby areas of brain resulting in further morbidity as well as increasing mortality risk. Lobectomies are also still considered as part of the surgical approach to intractable epilepsy (i.e., frontal and/or temporal).

Historical Background

Lobectomies of the brain for treatment of seizures have been studied the most. These procedures are performed when the subject does not respond to medication, or is unable to tolerate medication side effects, or has seizures caused by structural abnormalities in the brain and usually involve the temporal or frontal lobes. The recognized behavioral changes that occur after these procedures can be expected after partial or total lobectomies for any indication.

Current Knowledge

Temporal Lobectomy: temporal lobe seizures are the most common seizure type in man and can be caused by a variety of inherited or acquired

conditions. As a therapeutic procedure, the temporal lobectomy can be very effective. After surgery, 60–70% of patients are free of seizures that impair consciousness or cause abnormal movements. Twenty to twenty-five percent of patients still have some complex partial or tonic-clonic seizures, but the number of seizures is reduced by more than 85%. Only 10–15% of patients have no clinically significant improvement. Research has shown that intelligence quotients improve after lobectomy. The average gain 6 years after operation was 3.6 verbal IQ (VIQ) points and 10.3 performance IQ (PIQ) points in left temporal lobe patients and 2.9 VIQ points and 7.7 PIQ points in right temporal lobe patients, respectively. Major predictors of improved performance at 6 years were initial higher level of performance and lower age at surgery. Some complications of the procedure that can occur include problems with reading and in speech, memory, and personality, severe depression, or elements of psychosis. Emotional perception and memory are especially sensitive to removal of the amygdala as a result of the procedure.

Frontal Lobectomy: frontal lobectomy is the second most common type of epilepsy surgery, after temporal lobectomy. The success rates for frontal lobectomy are not as good as those for temporal lobectomy. After a frontal lobectomy, only 30–50% of patients are free of seizures that impair consciousness or cause abnormal movements. Twenty to forty percent of patients continue to have some complex partial or tonic-clonic seizures, but they are reduced by at least 90%. Twenty to thirty percent of patients have no worthwhile improvement. Although the results are not as good as with temporal lobectomy, at least 70% of patients who have had a frontal lobectomy enjoy a great improvement in seizure control. Most patients need to continue taking seizure medicines, but they may need to take less. Some complications of the procedure that can occur include changes in certain kinds of behavior. Patients who have a frontal lobectomy risk experiencing changes in personality,

motivation, the ability to plan and follow a process with several steps, the ability to organize actions over time, social graces, and the ability to behave appropriately for the social situation. Some mild changes in these areas may have begun before the surgery, as a result of the seizures that began in the frontal lobes.

Cross-References

- ▶ [Biopsy](#)
- ▶ [Temporal Lobectomy](#)

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Localization

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Definition

The theory of localization in the brain states that specific parts of the brain control specific aspects of brain function.

Current Knowledge

Localization of function in the brain refers to the theory that specific parts of the brain control specific aspects of brain function. The idea of a localization of function in the brain has been considered for hundreds of years. The now-debunked pseudoscience of phrenology was based on the idea that brain function was localized to specific parts of the brain and a phrenologist could analyze a person's specific brain function by examining the shape of the skull. Modern understanding of the brain is much more sophisticated, yet it is known that some brain functions are indeed localized.

The scientific community began accepting theories of localization when researchers Paul Broca, Carl Wernicke, and others discovered that damage to a specific part of the brain was associated with loss of specific functions. Paul Broca's research showed that damage to a specific part of the brain (the left frontal lobe) was associated with speech impairment. In the 1870s, Carl Wernicke found that a specific part of the brain (upper posterior temporal lobe) was responsible for speech reception. In 1870, Gustav Fritsch and J. L. Hitzig discovered the motor cortex when they found stimulating different parts of the cortex resulted in movement in certain body parts.

Today, many brain locations have been identified to have specific functions. In addition to the speech and motor areas already outlined, Table 1

Localization, Table 1 Functions of specific brain structures

Function	Location
Motor (execution of voluntary movement)	Primary motor cortex (posterior frontal lobe)
Somatosensory (sensory perception including temperature, pressure, pain, and body position)	Primary somatosensory cortex (postcentral gyrus)
Vision	Primary visual cortex (occipital lobe)
Auditory	Primary auditory cortex (Brodman areas 41 & 42)
Limbic functions (regulation of emotions)	Limbic system (some structures include amygdala, hippocampus, hypothalamus, and thalamus)

outlines some specific brain structures that have specific functions.

While it is widely accepted that localization of function is present in the brain, the extent of interconnectivity of these areas is not completely understood.

Cross-References

- [Frontal Lobe](#)
- [Limbic System](#)
- [Occipital Lobe](#)
- [Parietal Lobe](#)
- [Postcentral Gyrus](#)
- [Precentral Gyrus](#)
- [Temporal Lobe](#)
- [Visual Cortex](#)

Locked-In Syndrome

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Synonyms

De-efferented state; Locked-in state

Definition

Locked-in syndrome refers to a clinical condition consisting of:

- Paralysis of all four limbs.
- Paralysis of bilateral facial musculature.
- Paralysis of oral and pharyngeal musculature.
- Paralysis of horizontal eye movements.
- Voluntary control of eyelids and vertical eye movements are usually preserved.
- Consciousness is preserved.

Categorization

- *Total:* No voluntary control of limbs, tongue, pharynx, face, or eye movements, with preserved consciousness.
- *Classic:* As described in definition.
- *Incomplete:* Some preserved horizontal eye movements or limb movements.

Epidemiology

Incidence and Prevalence Locked-in syndrome is a rare disorder. There is no good data regarding the incidence or prevalence of locked-in syndrome.

Etiology The most common cause of locked-in syndrome is stroke, either an infarction or hemorrhage in the pons. Other causes are trauma, tumors of the brain stem, central pontine myelinolysis (CPM), Guillain-Barre syndrome (GBS), and multiple sclerosis (MS).

- The onset is acute in stroke.
- Traumatic cases may have additional cognitive impairments.
- Brainstem tumors have a gradual onset in most cases unless there is a hemorrhage into the tumor.
- GBS presents with an ascending paralysis.
- CPM is associated with electrolyte abnormalities.

In MS, the onset is slow and stepwise, due to cumulative demyelinating episodes.

Natural History, Prognostic Factors, and Outcomes

The term “locked-in syndrome” was first used in Plum and Posner’s *Diagnosis of Stupor and Coma*, First Edition, 1966.

Clinical In locked-in syndrome due to stroke, there is often an initial period of coma. Inconsistent responsiveness following this may lead to a diagnosis of minimally conscious state (MCS). The mean time to diagnosis has been reported as 2.5 months. More than half the time, a family member has been the first to recognize that the patient is aware and capable of communication.

Because of the more gradual onset, errors in the evaluation of cognitive state are less common in other etiologies.

Demographics Locked-in syndrome has been reported in all ages between the first and eighth decades of life. Average age of onset is between 33 and 46 years. Men are more often affected than women.

Survival Mortality is greatest in the first 4 months after onset and greater in vascular cases than in those with other causes. In one published study, 5-year survival was 83%, 10-year survival was 83%, and 20-year survival was 40%. The most common causes of death are infection (pneumonia, sepsis) and pulmonary embolus.

Prognosis Because this is such a rare disorder, and diagnosis is often delayed, there is no good information on early predictors of outcome in the vascular category. In the Copenhagen Stroke Study, patients with severe strokes (any location) had a better prognosis if they were young, had early recovery (in the first week), had no fever on admission, and had a caregiver at home (Jorgensen et al. 1999). In a retrospective study of basilar artery strokes, predictors of poor outcome (death or severe disability) were impaired

consciousness on admission or dysarthria, pupillary disorders, and lower cranial nerve involvement (Devuysy et al. 2002).

In vascular locked-in syndrome, improved survival has been reported with early rehabilitation (within the first month).

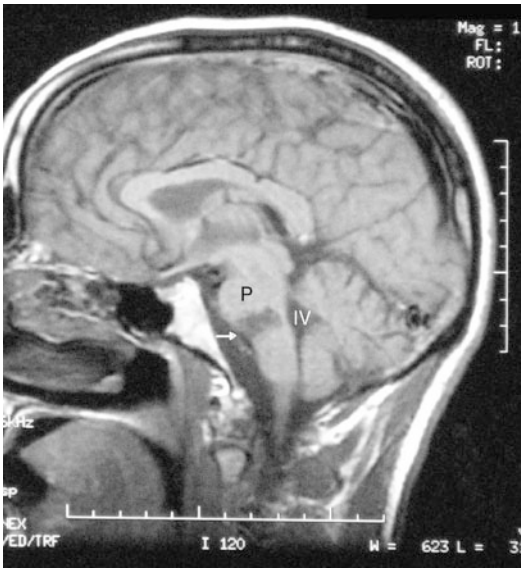
- In Guillain-Barre, treatment is available and recovery is expected.
- CPM is preventable, due to the over rapid correction of a low sodium level.
- In brainstem tumors, prognosis depends on the type of tumor.

Case History A 43-year-old male presented to the emergency room complaining of dizziness and vomiting, followed by inability to speak. CT scan was negative. He was thought to be having a panic attack and was given antianxiety medication. He was later found to have bilateral facial weakness and quadriparesis and required intubation. MRI revealed an infarction in the pons, and MRA revealed occlusion of the basilar artery (Figs. 1 and 2). He was admitted to hospital-level rehabilitation 1 month after onset. He communicated by eye blinks for “yes” and “no.” He was cognitively intact and participated in decision-making regarding his care. Over several months, he recovered the ability to move one index finger.

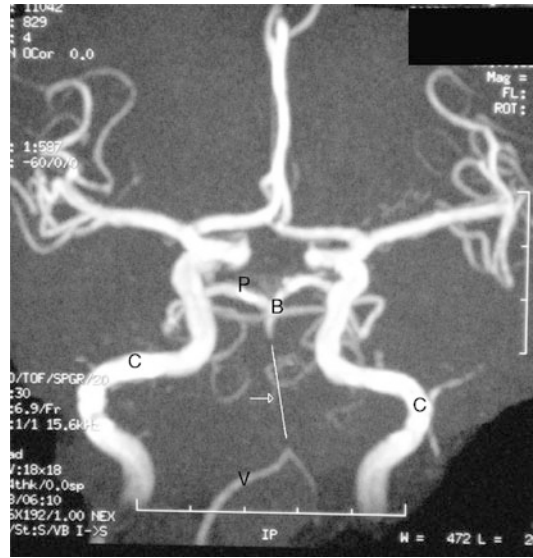
Neuropsychology and Psychology of Locked-In Syndrome

Neuropsychology Cognition is normal on neuropsychological testing in patients with locked-in syndrome, if there are no other additional brain lesions. In the first few months after injury, attention may be impaired. Fatigue may be a factor in neuropsychological evaluation, and several shorter evaluations will yield more reliable results than a full evaluation in a single session.

The neuropsychologist evaluating a patient with locked-in syndrome should prepare all the testing in advance in a yes/no format and before any evaluation begins, establish a mutually agreed



Locked-In Syndrome, Fig. 1 MRI, sagittal section of brain. The white arrow points to an area of infarction in the lower pons (*P*) that caused a case of locked-in syndrome. This area contains descending corticobulbar and corticospinal fibers, as well as the nuclei of the VI (abducens) nerve and VII (facial) nerve. The dorsal portion of the pons abutting the fourth ventricle (IV) is spared, allowing preservation of consciousness and normal sleep/wake cycles



Locked-In Syndrome, Fig. 2 The infarction seen in Fig. 1 was caused by a complete occlusion of the basilar artery. The vertebral arteries are smaller than normal (*V*: right vertebral artery). The carotid arteries are of normal size (*C*). The white line (open arrowhead) indicates the normal position of the basilar artery, which ends by forming the two posterior cerebral arteries (*P*: right posterior cerebral artery). A small remnant of the top of the basilar artery (*B*) remains

upon response (i.e., one blink means “yes,” two blinks means “no,” or other indicators that are reliable and reproducible).

Psychology Many people may think that death would be preferable to having locked-in syndrome. Families at times are counseled to withhold care. Evaluations of patients who have locked-in syndrome indicate that nearly half rate their mood as good. One study found that of 12 patients surviving > 10 years, none had a DNR order. Pain is correlated with suicidal thoughts, and adequate pain management is important in maintaining quality of life.

Evaluation

Initial evaluation is the same for all patients with acute onset of coma or impaired level of consciousness: history, physical exam, lab work

(kidney function, liver function, blood counts, evaluation for infection, drug testing), and CT scan. CT scans are done first because they are more widely available, and faster, but less sensitive to brainstem lesions than MRI. EEG may be indicated if there is suspicion of nonconvulsive status epilepticus.

If a pontine infarction is found, all involved clinicians need to be aware that there is a possibility of consciousness and attempt to communicate through whatever voluntary movement is present. Impaired level of consciousness may be present in the initial weeks, but attempts at communication should be done frequently.

Treatment

Initial management includes maintenance of respiratory function (mechanical ventilation, tracheotomy), treatment of infections (pneumonia,

urinary tract infections), prevention of deep vein thrombosis and pulmonary embolism, adequate nutrition/hydration (gastrostomy tube), and prevention of skin breakdown (pressure sores/decubitus ulcers).

All staff should be educated about the possibility of consciousness and methods to establish communication.

Rehabilitation should begin as soon as possible in a facility with experience in dealing with patients with impaired levels of alertness. Initial communication with a yes/no strategy can be augmented with the use of an alphabet board. Infrared eye movement sensors can be used to control computers and expand the communication abilities of patients with locked-in syndrome. The recovery of any movement that could control a call light or activate a computer could be facilitated by the use of functional electrical stimulation (FES) or robotic rehabilitation devices. Electrode grids implanted onto the cortex can control computers and direct the movement of powered wheelchairs, but at present this is experimental.

Cross-References

- ▶ [Guillain-Barré Syndrome](#)
- ▶ [Minimally Conscious State](#)

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Lockett v. Ohio (1978)

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Definition

The US Supreme Court ruled in *Lockett v. Ohio* (1978) that in the case of a defendant facing the death penalty, one is allowed to present *any aspect of character or record or any circumstance related to the offense* that could create a basis for a lesser sentence than the death penalty. The 8th and 14th Amendments of the Constitution required, in all but the rarest capital cases, that the triers of fact be allowed to consider a number of mitigating factors, both statutory and non-statutory, before imposing the death penalty. The Court held that the Ohio statute did not permit the type of individualized consideration of mitigating factors required by the Constitution. Despite this decision in favor of presenting mitigating factors, certain arguments have not been allowed to be presented by the defendant. Specifically, issues related to the morality of the death penalty and issues related to the execution process have not been allowed in any court.

Historical Background

Sandra Lockett was found guilty of capital murder in Ohio, a state in which she was limited in her ability to introduce mitigating evidence during the sentencing phase of her trial. She challenged the constitutionality of this limitation, in part, arguing that she was deprived the opportunity to fully inform the jury as to those factors that they may have considered that would have returned a penalty other than death. In *Lockett v. Ohio* (1978), the Court held (in a 6–2 vote) that the sentencer could “. . . not be precluded from considering as a mitigating factor, any aspect of the defendant’s character or record and any circumstances of the offense that the defendant offers as a basis for a

sentence of less than death.” As a result of the ruling, a defendant in a capital case cannot be limited in the type of mitigation he or she offers during the penalty phase of the trial. Any information regarding the defendant’s background, as a child or as an adult, could be considered relevant. Thus, factors such as a history of childhood trauma (e.g., physical or sexual abuse), verbal abuse, exposure to drugs and alcohol, neglect and abandonment, undiagnosed or misdiagnosed conditions (e.g., mental retardation, emotional disturbance, learning disability, ADHD), gang or cult membership, or witnessing the death of a family member or friend could be considered nonstatutory mitigation. In addition, any circumstances related to the crime could be considered mitigating. Lockett requires defense attorneys and forensic psychological and psychiatric experts to explore all avenues of mitigation because the factors that can be introduced are not limited to those specifically delineated by statute.

Cross-References

- ▶ [Atkins v. Virginia](#)
- ▶ [Death Penalty](#)
- ▶ [Mitigating Factors](#)

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Locus Ceruleus

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Synonyms

Blue spot; Nucleus pigmentosus pontis

Definition

Locus ceruleus (Latin, “place, dark blue”) is a pigmented noradrenergic nucleus located in the dorsorostral pons.

Current Knowledge

Locus ceruleus (also spelled *locus coeruleus*) contains 30,000–35,000 neurons and is made up of four subnuclei: central (largest), anterior, ventral, and posterior dorsal. The locus ceruleus is dark blue in sections; melanin granules inside the pigmented cells of locus ceruleus contribute to its blue color. The neurons of the locus ceruleus provide noradrenergic innervations to most regions of the central nervous system. The projections of the locus ceruleus include the spinal cord, brain stem, cerebellum, thalamic relay nuclei, amygdala, basal telencephalon, and cortex. The norepinephrine from the locus ceruleus has an excitatory effect on most of the brain, mediating arousal and attention processing. The locus ceruleus is targeted by several endogenous opioid peptides, e.g., enkephalin, excitatory amino acids, and stress-related peptides including corticotropin-releasing hormone. The locus ceruleus receives afferents from the hypothalamus including recently discovered orexin/hypocretin inputs, cerebellum, raphe nuclei, medial prefrontal cortex, nucleus paragigantocellularis, and nucleus prepositus hypoglossi. The cingulate gyrus and the amygdala also innervate the locus ceruleus, allowing emotional pain and stressors to trigger noradrenergic responses. Serotonin

and histamine fiber innervations of the locus ceruleus have been also described, the latter originates in the tuberomammillary nucleus.

The locus ceruleus is responsible for physiological responses to stress and panic and is involved in the mechanisms of clinical depression and mood disorders, panic disorder, and anxiety. The locus ceruleus is activated by stress and responds by increasing norepinephrine secretion, which in turn increases cognitive function (through the prefrontal cortex), increases motivation (through the nucleus accumbens), activates the hypothalamic-pituitary-adrenal axis, and increases the sympathetic discharge/inhibits parasympathetic tone (through the brain stem). Enhanced noradrenergic postsynaptic responsiveness in the neuronal pathway that originates in the locus ceruleus and ends in the basolateral nuclei of the amygdala is a major factor in the pathophysiology of most stress-induced fear circuitry disorders and especially of posttraumatic stress disorder (PTSD). Implications of the locus ceruleus in cognition, attention, and memory appear to be of particular interest for understanding such psychiatric disorders as attention deficit hyperactivity disorder (ADHD), Parkinson's and Alzheimer's diseases, schizophrenia, and dementia. The locus ceruleus is also involved in the rapid eye movement (REM) stage of sleep and is studied in relation to sleep disorders with a special attention given to regulation of locus ceruleus neurons by hypothalamic neuropeptide hypocretin. A number of behavioral studies indicated a critical role of noradrenergic neurons of the locus ceruleus in relapse and vulnerability to opiate abuse.

Cross-References

- [Arousal](#)
- [Stress](#)

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Loewenstein Occupational Therapy Cognitive Assessment

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Synonyms

LOTCA; LOTCA-G

Description

The Loewenstein Occupational Therapy Cognitive Assessment (LOTCA) battery – second edition. The LOTCA is a battery that provides an initial profile of the cognitive abilities of the brain-injured individual (TBI) stroke. It can also be used with SCI, dementia, central nervous system dysfunction, and learning disabilities. The tool was developed in Israel; however, it is frequently used in the United States. The battery takes 30–45 min to administer. It is used to assess if the patient can carry out everyday tasks.

The current edition (second) is divided into six main areas: (1) orientation, (2) visual perception, (3) spatial perception, (4) motor praxis, (5) visuomotor organization, and (6) thinking operations. The battery contains 26 subtests including the Riska Object Classification (ROC) (Williams and Allen 1985), which was added to enhance the evaluation of the categorization operation. This revised edition includes four major changes from the original version which were based on clinical experience and research results. Changes and additions were made to the following categories: orientation, spatial perception and motor praxis, categorization, and logic questions.

The LOTCA can be used for ages 6–70 and the LOTCA-G is for the geriatric population.

Historical Background

The LOTCA was developed by the staff members at the Occupational Therapy department at Loewenstein Rehabilitation Hospital (LRH) in Israel for the purpose of evaluating basic cognitive abilities in brain injury. Since its introduction in 1989, it has been widely used by occupational therapists with varied populations. Although the LOTCA was originally developed for clients with brain damage (traumatic brain injury, stroke, and brain tumors), it is also suitable for assessment in other populations where a cognitive status has to be established (spinal cord injury, degenerative and psychiatric diseases, and underachieving students).

Psychometric Data

Research data on reliability and validity of the LOTCA battery, which was established on adults with brain damage compared to normals, is also available on the performance of children in the age range of 6–12 years that verifies the hierarchical order of acquiring the cognitive competencies tested in the battery.

Inter-rater Reliability – collected two ways prior to data collection. Spearman's rank correlation coefficient showed inter-rater reliability ranging from 0.82 to 0.97 for the various subtests. Second, a video recording of the assessment of one client was viewed and scored by six therapists. Agreement reached 100% for 14 subtests, 86% for 4 subtests and 72% for 1 subtest, equaling an 86% level of agreement.

Internal Consistency Reliability – Cronbach's alpha coefficient was calculated for three areas included in the battery. An alpha coefficient of 0.87 was found for "perception" consisting of five subtests (object identification, shape identification, overlapping figures, object constancy, and spatial perception). An alpha coefficient of 0.95 was calculated for "visuomotor organization" consisting of eight subtests (praxis, copying geometric forms,

reproduction of models, constructing a pegboard design, constructing a colored block design, constructing a plain block design, reproduction of a puzzle, and drawing a clock). The third area, "thinking operations," consisting of five subtests, (categorization, structured and unstructured ROC classifications, pictorial sequence, and geometrical sequence) showed an alpha coefficient of 0.85. (At the time of study, only the first pictorial sequence was included.)

Correlation coefficients range from 0.40 to 0.80 among the subtests suggest that they are not all equivalent, and it is therefore expedient to retain all parts of the battery.

Clinical Uses

The LOTCA offers a quick, relatively simple battery that is useful in identifying cognitive dysfunction and also provides a profile of the client's cognitive status useful for establishing a baseline for treatment, planning treatment goals, and monitoring cognitive/functional changes during treatment. It can provide some groundwork for the neuropsychologist's assessment. The test battery is based on Loewenstein's occupational therapists' clinical experience as well as on cognitive neuropsychology and developmental theories (Luria 1980; Golden 1984; Piaget and Inhelder 1964). The LOTCA can also be used as a follow-up tool.

See Also

► [Occupational Therapy](#)

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Logopenic Aphasia

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Synonyms

Primary progressive aphasia

Short Description or Definition

The term logopenic aphasia refers to a type of progressive aphasia characterized by word-finding problems and slowed rate of verbal output, grammatically simple but correct speech, and preserved comprehension. Patients with logopenic aphasia differ from those characterized as “nonfluent” by better conversational speech, and from those characterized as “semantic” by preserved comprehension.

Categorization

The term logopenic aphasia has been in the literature for many years, but was first operationalized by Gorno-Tempini (Gorno-Tempini et al. 2004), who proposed a classification system based on presenting

language symptoms, distinctive patterns of brain atrophy and genetic factors. The logopenic subtype is defined as having the following characteristics:

1. Lowest score on tests of syntactic comprehension
2. Impaired naming performance (first percentile), but with preserved recognition
3. Impaired repetition
4. Impaired single word reading
5. Intermediate performance on fluency tests
6. Intact single word comprehension
7. Intact semantic associations

This term was later refined and described as a subtype of primary progressive aphasia (PPA) (Rogalski and Mesulam 2007) with the following clinical presentation: word-finding pauses (patient may be nonfluent when asked to describe specific information); fluent speech during small talk (often involving circumlocutions); impaired object naming (usually); and relatively preserved speech syntax and single word comprehension. As with the other subtypes of PPA, additional diagnostic criteria include:

1. Presence of a language disorder as characterized by one or more of the following: word-finding deficits that cannot be attributed to dysarthria; object naming impairments; poor syntax in spoken or written language; and spelling errors.
2. Evidence of indolent progression.
3. Relative preservation of memory for recent events, familiar face and object recognition, behavior and basic personality for approximately the first 2 years.
4. Imaging evidence that the cause is not a space-occupying or cerebrovascular lesion.

Epidemiology

Of all the progressive aphasia subtypes, the logopenic variant is the most likely to be associated with Alzheimer’s disease pathology (Josephs et al. 2008; Kertesz et al. 2005; Mesulam et al. 2008), although the next most common pathology is frontotemporal lobar degeneration (FTLD) with tau-negative pathology but ubiquitin containing

inclusions. Genetically, this variant has the highest rate of APOE e4 allele (a known risk factor for Alzheimer’s disease) compared to nonfluent and semantic types (Gorno-Tempini et al. 2004).

Neuropsychology and Psychology of Logopenic Aphasia

A thorough evaluation of all facets of speech and language will help to differentiate the logopenic subtype from other forms of progressive aphasia. Motor speech, grammar, and single word comprehension are spared early in the course of logopenic progressive aphasia (LPA) and Table 1 lists common language tests by domain as well as the expected performance of LPA patients compared to that of patients with other forms of progressive aphasia (i.e., semantic dementia [SD] and non-fluent progressive aphasia [NPFA]).

Evaluation

In general, patients with any subtype of progressive aphasia are most likely to show anatomical involvement of the left hemisphere. Using voxel-based morphometry, logopenic patients showed significant atrophy in the posterior portion of the left middle and superior temporal gyrus and the inferior parietal compared to control subjects (Gorno-Tempini et al. 2008). In another study comparing LPA to other aphasia subtypes, additional areas of relatively greater atrophy were also found in the left anterior hippocampus and precuneus regions (Gorno-Tempini et al. 2004). Compared to other subtypes of progressive aphasia and the behavioral variant of frontotemporal dementia, the logopenic subtype has been shown to have slightly greater annualized brain volume loss (Knopman et al. 2009) and

Logopenic Aphasia, Table 1 Common tests used to evaluate language areas

Skill tested	Description of LPA	Comparison
Fluency	Slowed speech, correct syntax, frequent word finding pauses	NPFA < LPA < SD
BDAE-3 ^a conversational and expository speech: 7 different discourse elements are scored		
WAB-R ^b spontaneous speech: Information content and fluency each scored on a 0–10 point scale		
Motor	Dysarthria uncommon; if apraxia is present usually mild	NPFA < LPA < SD
Motor speech evaluation (Wertz et al. 1984): Dysarthria and apraxia of speech scored on a 1–7 points scale on different tasks		
Apraxia battery for Adults-2 (Dabul 2000): Six subtests measuring both limb and oral apraxia, and articulation		
Auditory comprehension		
Word	Generally intact	SD < LPA < NPFA
BDAE-3 word comprehension: 16 items (short forms) or 37 items (standard form) pictured on cards. Extended testing includes 10 items in each of the following groups: Foods, tools, and animals		
WAB-R auditory word recognition: 60 items (real and pictured) broken into 10 categories		
Sentence	Impaired for syntactically complex information	LPA < NPFA < SD
BDAE-3 complex ideational material: Yes/no questions using syntactically complex sentence structure		
WAB-R commands: 11 items of progressively longer and more complex grammatical structure		
Reading	Impaired oral reading of both regular and irregular words	LPA = NPFA = SD
PALPA ^c regularity and reading subtest: Reading aloud of regular, exceptional, and non-words		
BDAE-3 oral reading: Standard form is 10 regular words; extended battery includes 12 mixed morphological type words (e.g., noisier) and 12 “semantic paralexia-prone” words (e.g., loyalty)		
Naming	Impaired naming, but recognition generally intact	SD < LPA < NPFA
Boston naming test (Kaplan et al. 2001): 15 items (short form) or 60 items (standard) ranging from easiest to most difficult; second edition includes a multiple choice recognition		
Repetition		NPFA < LPA < SD
WAB-R repetition: 15 items ranging from words to complex sentences		
BDAE-3 repetition: 3 subtests including single words, nonsense words, and sentences		

^aBoston Diagnostic Aphasia Examination (BDAE-3; Goodglass et al. 2001)
^bWestern Aphasia Battery Revised (WAB-R; Kertesz 2007)
^cPsycholinguistic Assessments of Language Processing in Aphasia (PALPA; Kay et al. 1992)

greater annualized decline on the mini mental state examination (Knopman et al. 2008).

Treatment

Patients with logopenic aphasia are more likely to be treated with cholinesterase inhibitors than other aphasia subtypes (Gorno-Tempini et al. 2008), possibly because of the increased finding of Alzheimer's disease pathology. However, there are no medications specifically approved for treating any type of progressive aphasia, and there have been no large-scale clinical trials using any known pharmacologic agents. Of the two small clinical trials conducted, neither one characterized the progressive aphasia patients by subtype. A trial of bromocriptine was negative (Reed et al. 2004), but a trend for a significant treatment effect was found in PPA subjects treated with galantamine for 8-weeks compared to placebo (Kertesz et al. 2008).

Cross-References

- [Frontotemporal Lobar Degenerations](#)
- [Progressive Aphasia](#)

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Logorrhea

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Synonyms

Press of speech

Definition

Logorrhea means excessive verbal production; it is manifested as an unusual verbosity that may suggest the presence of neurological or psychiatric pathologies. Logorrhea is frequently reported as a symptom of Wernicke's aphasia, where damage to

the posterior language cortex yields reduced verbal self-monitoring and a press for speech despite anomia and the consequent absence of meaningful linguistic content in spoken utterances (Christman and Buckingham 1989). Logorrhea in aphasia may be produced with normal prosody and a normal or slightly fast speech rate, and it may co-occur with neologistic jargon (Hallowell and Chapey 2008). Logorrhea has also been reported as a symptom of mania in bipolar disorder and as a symptom of chronic speech catatonia syndrome (Lee 2004).

Cross-References

- ▶ [Catatonic Behavior](#)
- ▶ [Jargon](#)
- ▶ [Wernicke's Aphasia](#)

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Lorazepam

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Generic Name

Lorazepam

Brand Name

Ativan

Class

Anxiolytic

Proposed Mechanism(s) of Action

Binds to benzodiazepine receptors at the GABA-A ligand-gated channel, thus allowing for neuronal hyperpolarization. Benzodiazepines enhance the inhibitory action of GABA via boosted chloride conductance. This inhibition in the cortex may provide lorazepam's therapeutic benefits in seizure disorders.

Indication

Anxiety, anxiety associated with depression, status epilepticus, and presurgical preanesthetic

Off-Label Use

Insomnia, muscle spasm, alcohol-induced psychosis, headache, panic disorder, acute mania, acute psychosis, and delirium

Side Effects

Sedation, dizziness, unsteadiness, weakness, fatigue, drowsiness, amnesia, confusion, disorientation, depression, suicidal ideation/attempt, vertigo, ataxia, sleep apnea, asthenia, EPS, respiratory depression, tremor, convulsions/seizures, visual disturbances, dysarthria, hypotension, blood dyscrasias, change in libido, impotence, and change in appetite

Serious

Respiratory depression, hepatic dysfunction (rare), renal dysfunction and blood dyscrasias, and grand mal seizures

Common

Sedation, fatigue, depression, dizziness, memory problems, disinhibition, confusion, ataxia, and slurred speech

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Additional Information

Drug interaction effects. http://www.drugs.com/drug_interactions.html

Drug molecule images. <http://www.worldofmolecules.com/drugs/>

Free drug online and PDA software. www.epocrates.com
Gene-based estimate of drug interactions. <http://mhcdailytondes.com:8080/cgi-bin/ddiD4?ver=4&task=getDrugList>

Pill identification. http://www.drugs.com/pill_identification.html

Loss of Consciousness

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Synonyms

Coma; Unconscious

Definition

Loss of consciousness (LOC) is defined as a significant alteration of mental status involving a lack of responsiveness to people and other environmental stimuli. It results in an interruption of one's self and surroundings. Examples include being in a comatose state or experiencing a temporary loss of consciousness such as a syncope episode or fainting. Prolonged LOC is called a vegetative state or persistent vegetative state. The amount of

time it takes a person to regain consciousness and awareness of one's surroundings is often used as an indication of brain injury severity. Individuals who experience LOC may not always be able to state the amount of time they were unconscious. LOC information is often collected in research studies and has been shown to be a good predictor of outcome. When a person cannot remember the scene or may have post-traumatic amnesia for the event, it is sometimes advisable to obtain information from eyewitnesses of the accident or injury. However, this too can be disputable at times if witnesses to trauma arrive late on the scene.

Current Knowledge

Causes

Causes for loss of consciousness can include traumatic brain injury, hypoxia, stroke, cardiac arrest, severe poisoning secondary to drug and alcohol overdoses, severe fatigue, central nervous system diseases, diabetic coma, and electrolyte imbalances, among others.

Cross-References

- [Acceleration Injury](#)
- [Coma](#)
- [Concussion](#)
- [Mild Traumatic Brain Injury](#)
- [Post-concussive Syndrome](#)
- [Sport-Related Concussion](#)
- [Traumatic Brain Injury \(TBI\)](#)

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Walter Reed National Military Medical Center,
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Name and Degrees

Louis M. French

- 2001–2003 Defense and Veterans Brain Injury Center, Department of Neurology, Walter Reed Army Medical Center Washington, DC. Postdoctoral Fellowship in Clinical Neuropsychology
- 2000–2001 George Washington University Medical Center/Defense and Veterans Head Injury Program, Walter Reed Army Medical Center Washington, DC. Internship in Clinical
- 1997–2000 National Institute of Mental Health, Section on Clinical and Experimental Neuropsychology, Laboratory of Brain and Cognition Bethesda, MD. Pre-Doctoral Fellowship in Neuropsychology
- 1996–2001 George Washington University Washington, DC. Psy.D. – Clinical Psychology Specialty Area: Assessment Thesis Title: The use of psychological tests in the course of psychotherapy
- 1985–1989 Loyola University (Maryland) Baltimore, MD. M.A., Clinical Psychology Thesis Title: Elizur's Rorschach content test – a measure of the sensitivity to life stress and depression
- 1981–1985 Loyola University in Maryland Baltimore, MD. B.A., English and Psychology (double major)

Major Appointments (Institution, Location, Dates)

- 2015-present: Deputy Director for Operations, National Intrepid Center of Excellence, Walter Reed National Military Medical Center (WRNMMC)
- 2010-present: Co-Director Phenotyping Core, Center for Neuroscience and Regenerative Medicine (CNRM)
- 2011-present: Site Director, Defense and Veterans Brain Injury Center (DVBIC), WRNMMC at Bethesda, MD
- 2007-present: Assistant Professor of Neurology, F. Edward Hebert School of Medicine, Uniformed Services University of the Health Sciences
- 2011–2015: Chief, Traumatic Brain Injury Service, WRNMMC
- 2007–2011: Director, Traumatic Brain Injury Program, Walter Reed Army Medical Center (WRAMC), Department of Orthopedics and Rehabilitation
- 2007: Ad Hoc Reviewer, Food and Drug Administration Orphan Products Development Program Member, Surgeon General's Task Force on Traumatic Brain Injury in the Army
- 2006–2011: Site Director, DVBIC, WRAMC, Washington DC
- 2005–2008: Training Director, Psychology Internship Training Program, DVBIC, Walter Reed
- 2004–2006: Chief, Clinical Services, DVBIC, WRAMC, Washington DC
- Member, Neurotrauma Scientific Steering Committee, Combat Casualty Care Program (JPC-6), US Army Medical Research and Materiel Command
- Reviewer, Department of Veterans Affairs Rehabilitation Research and Development Service

Major Honors and Awards

- Intramural Research Training Award, National Institutes of Health (1997)

- National Honor Society in Psychology, Psi Chi (1989)
- District of Columbia Metropolitan Police Department Chief of Police Medal of Merit (2008)

Landmark Clinical, Scientific, and Professional Contributions

- DVBIC 2008–2009: Principal Investigator; Military Blast-Related Traumatic Brain Injury: A Study of Neuroanatomical and Neurobehavioral Sequelae and Low Cost Clinical Intervention.
- DVBIC 2008–2011: Principal Investigator; Traumatic Brain Injury and Substance Use Disorders Among Injured Soldiers.
- DVBIC 2009: Principal Investigator; DVBIC WRAMC Prospective Traumatic Brain Injury Tracking Protocol.
- Amputee Coalition of America 2009–2012: Principal Investigator; A Demonstration Program to Test the Efficacy of Peer Visitation for Caregivers of Veterans of Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) with Polytrauma/Blast-Related Injury.
- CNRM 2009–2012: Principal Investigator; A randomized, controlled pilot study looking at the effectiveness and feasibility of novel rehabilitation approaches for Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) patients with persistent complaints of cognitive dysfunction following a traumatic brain injury.
- CDMRP 2009–2012: Associate Investigator; A Randomized Exploratory Study to Evaluate Two Acupuncture Methods for the Treatment of Headaches Associated with TBI
- CDMRP and CNRM 2009–2013: Associate Investigator; National Capital Consortium TBI Neuroimaging Core Project
- WRAMC 2010: Associate Investigator; Characterizing High Velocity Angular Vestibulo-ocular reflex function in Service Members Post Blast Exposure
- CDMRP 2010–2011: Associate Investigator Epigenetic Patterns of TBI: DNA Methylation in Serum of OIF/OEF Service Members – An Exploratory Case Control Study
- CDMRP 2010–2012: Associate Investigator; An fMRI Study of TBI Associated with Blast Injury
- CDMRP/InTrust: Associate Investigator; Brain Indices of Risk for PTSD after Mild TBI
- CNRM and DVBIC 2011–2013: Principal Investigator Exploring the Natural History of Traumatic Brain Injury within a Military Cohort – A Longitudinal Database and Blood Banking Study
- CNRM 2014–2016: Associate Investigator; A pilot study of TMS to treat the symptoms of mTBI and PTSD

Short Biography

Louis M. French, PsyD, is the Deputy Director for Operations at the National Intrepid Center of Excellence (NICoE) (<http://www.wrnmcc.capmed.mil/NICoE/SitePages/index.aspx>), at the Walter Reed National Military Medical Center (WRNMMC). He served as the Chief, Traumatic Brain Injury (TBI) at Walter Reed Army Medical Center (prior to the integration of Walter Reed and National Naval Medical Center) and at WRNMMC, prior to the integration of all TBI services on the WRNMMC campus in late 2014. He chairs the Joint Traumatic Brain Injury Task Force which coordinates TBI care in the National Capitol Region Medical Directorate of the Department of Defense (DoD). He is also the site director for the Defense and Veterans Brain Injury Center (DVBIC) at WRNMMC (<http://dvbic.dcoe.mil/location/walter-reed-nmmc-md>), the largest site in that network. He is responsible for overseeing all aspects of the screening, assessment, and rehabilitation of those with TBI at the flagship military care facility in the DoD network. He holds faculty positions in the Departments of Neurology and Rehabilitation at the Uniformed Services University of the Health Sciences.

Dr. French received his doctorate in clinical psychology, focused on assessment, from the George Washington University. He completed fellowships in clinical and experimental neuropsychology at the National Institute of Mental Health and in neuropsychology, focusing on TBI, at the DVBIC at Walter Reed Army Medical Center.

In his current role, Dr. French has participated in multiple Federal panels and workgroups about TBI in the military, helping to shape current policy on screening and treatment for TBI on the battlefield and at home. These included the Army Surgeon General's Taskforce on TBI, whose report provided the foundation for the structure of TBI screening and treatment that is currently in place in the DoD. He was one of the authors who reshaped the Standardized Assessment of Concussion (SAC) to construct the Military Acute Concussion Evaluation (MACE) (<http://dvbic.dcoe.mil/research/military-acute-concussion-evaluation-mace>), which is the standard for concussion screening in the military.

At WRNMMC, he participates in a diversified research portfolio. He is principal investigator on multiple studies of TBI in returning Service Members, including the Congressionally mandated 15-year natural history of TBI in military service members study. He is a lead investigator and co-Director of the Phenotyping Core with the Center for Neuroscience and Regenerative Medicine (CNRM) (<https://www.usuhs.edu/cnrm/>) a program that integrates research efforts on TBI and Post-traumatic Stress Disorder (PTSD) between the DoD and the National Institutes of Health. He has published over 70 peer-reviewed journal articles and book chapters in the area of military TBI and neuropsychology.

See Also

- [Defense and Veterans Brain Injury Center](#)
- [Department of Defense \(DoD\)](#)
- [Military Acute Concussion Evaluation](#)
- [National Intrepid Center of Excellence](#)

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L-Tryptophan

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Synonyms

5-HTP; 5-hydroxytryptophan; Trp; Tryptophan; W

Indications and Definition

The term is sometimes used interchangeably with the term “tryptophan” and abbreviated “Trp” or “W.” L-Tryptophan is one of the nine essential amino acids available in most protein-based foods. Essential amino acids must be derived from food or supplements. Nonessential amino acids can be synthesized from essential or other nonessential amino acids. During digestion, L-tryptophan is broken down by intestinal bacteria that cause the odor associated with fecal material. The L-isomer from tryptophan contains the organic structural heterocyclic, indole, distinguishing it from tryptophan’s d-isomer. The L-isomer comprises the structure of the protein (IUPAC-IUB-JCBN 1983; L-Tryptophan 2009).

L-Tryptophan can be synthetically and organically derived. Synthetically, it is formulated from the bacterium, *Escherichia coli*, and the fermentation of serine, a nonessential organic polar amino acid, and indole. Tryptophan-synthase then converts this to tryptophan.

Mechanisms of Action

L-Tryptophan is the biochemical precursor for many compounds, including serotonin, melatonin, and niacin. It is converted to 5-HTP by the enzyme, tryptophan hydroxylase. 5-HTP (oxitriptan), the intermediary between tryptophan and serotonin, is decarboxylated to 5-hydroxytryptamine (5-HT) or serotonin via aromatic-L-amino acid decarboxylase. The vitamin B6 assists this conversion.

5-HTP is psychoactive and readily crosses the blood-brain barrier (BBB), whereas 5-HT (serotonin) does not. 5-HTP and five other amino acids (tyrosine, phenylalanine, valine, leucine, and isoleucine) bind to transport molecules to cross the BBB. High levels of the 5-HTP are believed to increase the synthesis of serotonin in the central nervous system. This increases the release and bioavailability of serotonin from the raphe nuclei (Sandyk 1992; Turner et al. 2006; Van Praag 1983).

Melatonin is released from the pineal gland as a function of the degradation of serotonin. The enzyme, *N*-acetyl-transferase, metabolizes serotonin into *N*-acetyl-5-HT, which is then methylated by 5-hydroxyindole-*O*-methyltransferase into melatonin.

L-Tryptophan is also a precursor of niacin synthesis in the kynurenine pathway. *N*-Formyl-kynurenine is converted to kynurenine via formamidase. Kynurenine pathway metabolism produces 2-amino-3-(3-oxoprop-1-enyl)-fumaric acid, which undergoes nonenzymatic cyclization, resulting in the production of niacin via the quinolinate pathway (L-Tryptophan 2009; Tryptophan 2003).

Specific Compounds and Properties

The chemical formula of L-tryptophan is $C_{11}H_{12}N_2O_2$. Its chemical weight is 204.2252 (Metabolomics Toolbox 2009).

Clinical Use

The metabolite of tryptophan, 5-hydroxytryptophan (5-HTP), is occasionally used in the prescription form, Tryptan, to augment antidepressant medication with treatment-resistant affective disorders. The non-pharmaceutical form of 5-HTP is sold as a dietary supplement in health food stores. It is marketed for the treatment of numerous conditions from suppressing appetite and inducing sleep to premenstrual dysphoric disorder, epilepsy, dementia, and depression. A 2001 meta-analysis suggested that its utility as an

antidepressant, sleep aid, and appetite suppression was not sufficiently demonstrated by adequate research methodologies to be considered efficacious. Research is lacking regarding the efficacy of tryptophan to treat epilepsy or dementia. The studies that have been completed have been inconclusive (5-Hydroxytryptophan 2009; IUPAC-IUB-JCBN 1983; L-Tryptophan 2009).

Research investigating the use of tryptophan for the symptoms of other conditions associated with low serotonin levels such as depression, seasonal affective disorder, and premenstrual dysphoric disorders has shown some promise, but more data are needed (L-Tryptophan 2009; Sandyk 1992; Turner et al. 2006; Van Praag 1983).

Tryptophan or 5-HTP is not regulated by the Food and Drug Administration (FDA), rendering standardization and research matters left to individual makers of the products. The quality and labeling accuracy of dietary and nutritional supplements vary considerably as a result (L-Tryptophan 2009).

Tryptophan Deficiency

In developed countries, tryptophan deficiency is not common but can occur among individuals with poor overall protein intake. A deficiency of tryptophan can lead to vitamin B3 deficiency and has been suggested in depression, insomnia, schizophrenia, suicidal thoughts, and carbohydrate craving. It has also been implicated as a possible factor when magnesium is also deficient, in cases involving heart artery spasms (Vitamin B3 2006). Tryptophan is rapidly metabolized into the toxic metabolites hydroxykynurenine, xanthurenic acid, and hydroxyanthranilic acid in individuals deficient in vitamin B6, reducing to less than 1% the bioavailability of ingested tryptophan to the brain. This can have considerable negative effects on energy, mood, sleep, and other functions thought to be mediated at least in part by tryptophan (L-Tryptophan 2009). Insufficient levels of tryptophan are also seen in fructose malabsorption, also called dietary fructose intolerance. Fructose malabsorption is a digestive

disorder of the small intestine whereby tryptophan cannot be adequately absorbed by intestinal tissue, resulting in excess levels of intestinal fructose. It has been estimated that 30–40% of the population in parts of central Europe are affected by fructose malabsorption (Fructose malabsorption 2009; L-Tryptophan 2009).

Side Effects

Research looking at the efficacy of 5-HTP to increase plasma serotonin levels when coadministered with a peripheral decarboxylase inhibitor such as carbidopa suggested it may decrease irritability, aggression, and movement disturbances associated with Parkinson's disease and dementia. However, other investigations raised concern that this combination may increase the risk of symptoms associated with the autoimmune disorder, scleroderma (5-Hydroxytryptophan 2009; South 2009).

Tryptophan ingested via typical dietary routes does not cause side effects. Tryptophan supplementation has been associated with difficulty breathing, hives, itching, rash, swelling of the mouth or throat, and wheezing. Potentially serious adverse reactions include serotonin syndrome and eosinophilia-myalgia syndrome (EMS), particularly if individuals are taking other serotonin-enhancing products (Monson and Schoenstadt 2008).

Dietary Sources

The most abundant sources of dietary tryptophan, a common constituent of most protein-based foods, are bananas, chick peas, chocolate, cottage cheese, dates, eggs, fish, mangoes, red meat, milk casein, oats, peanuts, poultry, pumpkin seeds, sunflower seeds, and yogurt (L-Tryptophan 2009). However, of all 22 amino acids, tryptophan is the least available. In a typical protein-based animal or vegetarian diet, only about 1–1.5 g of tryptophan per day is ingested.

Turkey is not a significantly better source of tryptophan than other poultries. However, it is commonly perceived to be the source of

drowsiness post the typical American Thanksgiving dinner. The turkey dinner-tryptophan connection has its origins in the science of carbohydrate metabolism. When foods rich in tryptophan are consumed as part of a high-carbohydrate meal, the insulin released stimulates muscle tissue cells to uptake branched chain large neutral amino acids (LNAA). This increases the ratio of tryptophan to LNAA which decreases competition for binding to the LNAA transporter. Relatively higher levels of tryptophan bind to the transporter molecule and cross the BBB where the conversion to serotonin and then melatonin occurs. Higher levels of serotonin and melatonin induce the sleepiness attributed to tryptophan in turkey (L-Tryptophan 2009).

History

Sir Frederick Hopkins in 1901 is credited with isolating the tryptophan molecule via casein hydrolysis. The USA banned the use of tryptophan as a dietary supplement in 1991 following a 1989 outbreak of the autoimmune condition, eosinophilia-myalgia syndrome (EMS). At least 37 died, and 1,500 were disabled following ingestion of L-tryptophan hypothesized to have contained trace impurities. The impurities were initially thought to have resulted from the methods of genetic engineering used by the Japanese supplier to synthesize the bacteria that produces L-tryptophan. Other epidemiological studies suggested that L-tryptophan metabolites produced during digestion as a function of normal histamine metabolism were inhibited. As a result, the ingestion of large doses of tryptophan was thought to cause excessive levels of histamine, increasing the susceptibility to EMS in vulnerable individuals (L-Tryptophan 2009). Despite remediation of purification procedures, the FDA maintained the ban on the sale of L-tryptophan, until 2001. In 2002, the dietary supplement, L-tryptophan, was sold again in the USA as a result of reduced marketing restrictions. The FDA maintained importation bans based on concerns that the causal factors for the EMS outbreak were not yet fully understood. The prescription

form of tryptophan, Tryptan, remained in the market (L-Tryptophan 2009).

Cross-References

- Serotonin
- Serotonin Syndrome
- L-Tryptophan

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Lumbar Puncture

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Synonyms

Lumbar tap; Spinal puncture; Spinal tap

Definition

Lumbar usually refers to that part of the back or spine between the ribs and the pelvis. Lumbar puncture (LP) used to be called a spinal puncture or in common parlance a “spinal tap.” Before CT scans were invented, the majority of the “neurological” exam would have consisted of a 2 or 3 h history and physical, appropriate X-rays, and a lumbar puncture. Lumbar punctures could generate headaches, infections, or worse (i.e., herniation). With the advent of the much less invasive CT and MRI brain scans, the importance of the lumbar puncture as a diagnostic or treatment tool has greatly declined. It is now especially used for the evaluation of infectious, malignant or immunological disorders. It also has been used to evaluate suspected hydrocephalus through serial taps and CSF drainage. Prior to any LP, the clinician must assure the absence of increased intracranial pressure to avoid possible downward brain herniation. A lumbar “tap” can also be used to assess for metastatic brain cancer, subarachnoid hemorrhage, or meningitis, among other conditions. It is also a procedure for injecting contrast agents or administering spinal anesthesia. An LP is usually done at the bedside and involves inserting a needle into the subarachnoid space of the spinal column. As a diagnostic test, samples of cerebrospinal fluid (CSF) are collected and analyzed for a variety of factors depending on the condition being assessed.

Current Knowledge

Spinal taps used to be a standard portion of the neurological evaluation. They are not performed nearly as frequently as in the past and only for special reasons as noted above.

Cross-References

- ▶ [Encephalopathy](#)
- ▶ [Hydrocephalus](#)
- ▶ [Multiple Sclerosis](#)

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Lupus Cerebritis

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Synonyms

CNS lupus

Definition

Lupus cerebritis is an important complication of systemic lupus erythematosus, characterized by cerebral vasculitis or inflammation of the blood vessels in the brain. This may result in stroke or other symptoms including headaches, seizures,

psychosis, dementia, or peripheral neuropathy. Stroke occurs in 5–20% of all patients with systemic lupus. It is treated by the control of systemic lupus and by the use of anti-inflammatory medications such as steroids.

Cross-References

- [Cerebral Angiitis](#)
- [Collagen Vascular Disease](#)
- [Vasculitis](#)

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Luria Nebraska Neuropsychological Battery

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Synonyms

LNNB; Luria-Nebraska Battery

Description

The LNNB, developed by Golden and his colleagues (Golden et al. 1991), was designed to more accurately discriminate patients with neurological impairments from normal individuals. It has a further goal of allowing for the lateralization and localization of neurological impairment. The LNNB consists of two forms: Form I contains 11 scales and Form II contains 12 scales. The two scales are supposed to serve as parallel forms with Form II

containing a measure that assesses delayed recall of some of the previously administered short-term memory items. Each item is scored from 0 (no impairment) to 2 (severe impairment). The scales are now relabeled C1–C12, replacing the scale names (e.g., *Motor Functions* or *Rhythm*), due to the fact that the scales are multidetermined, which makes the labels less meaningful. Five summary scales have been created using items from the clinical scales. The *Pathognomic* scale consists of items designed to discriminate patients with neurological impairment from healthy individuals. The *right hemisphere* and *left hemisphere* scales consist of tactile and motor functions designed to lateralize dysfunction. The *Profile Elevation* and *Impairment* scales are designed to determine the patient's level of functioning and extent of impairment (Lezak 2012).

Additional scales have been added to the LNNB since it was first developed. These include 8 localizations scales, 4 for each side of the brain (e.g., frontal and parietal-occipital), and 28 factor scales (e.g., four for reading). Another addition to the LNNB is a 66-item list of qualitative aspects of test performance designed to aid the examiner in evaluating the nature of the patient's failure on a particular task, not merely to document its occurrence (Lezak 2012).

A short form of the LNNB was developed by McCue and colleagues (1985). This form was proposed for use with elderly patients. It retains the complete Memory, Intellectual Processes, and Pathognomic scales, drops the Rhythm scale, and reduces the number of items on all other scales, leaving 141 total items. Differences between the standard and short forms of the LNNB were found with the short form showing lower (i.e., better) scores on the Expressive Language scale and higher (i.e., worse) scores on Reading. The short form was able to correctly identify approximately 75% of Alzheimer patients and 90% of depressed elderly patients, when LNNB age and education corrections were entered into scale calculations.

Historical Background

The LNNB is based on the work of A. L. Christensen (1979). She took Luria's examination

techniques and test materials, as presented in works such as *Higher Cortical Functions in Man* (Luria 1966), and organized them under a single battery. The materials and techniques incorporated into the battery spanned the range of methods that Luria incorporated into his investigations (e.g., higher kinaesthetic and coetaneous functions; 1966). In keeping with the spirit of Lurian investigation, Christensen stressed the need to understand how the patient arrived at a response while downplaying the importance of standard scores. As with other approaches based on Luria's theories (e.g., Boston Process Approach; Kaplan 1990), Christensen emphasized the importance of tailoring the procedures in a manner that will challenge, but not overly frustrate, the patient.

The main advantage of Christensen's battery is that it enables actual observation of behavior rather than inferred cognitive processes. It is also inexpensive, flexible, and brief to administer (Lezak 2012). A number of drawbacks limit the utility of the battery. First, as reviewed by Lezak (2012), the battery lacks tests of attention, concentration, and mental tracking. Moreover, there is a dearth of techniques available to assess non-verbal memory and concept formation, while there are no methods of evaluating fund of information. A further limitation is that the techniques incorporated into the battery, while useful in discriminating patients with severe impairments, are not useful in detecting most mild or diffuse deficits.

The LNNB was developed, in part, as a way to standardize the items in Christensen's battery (Golden et al. 1991).

Psychometric Data

The norms for Form I of the LNNB were based on 50 subjects (26 women and 24 men) hospitalized for a range of medical conditions (e.g., back injuries, infectious diseases, and chronic pain) with an average age of 42 years and 12.2 years of education. Form II was standardized on 51 normal individuals (Golden et al. 1991). The *critical level*, which provides the cutting score for the clinical

scales, is derived by multiplying the patient's age by 0.214 for every year between 25 and 70 years. Correction for education is done by multiplying the years of education (0–20) by 1.47 and subtracting this number from the critical level. A criticism of this approach is that age and education are treated as linear variables, with no accommodation for the potential differential impact that these variables can have on various tasks. Furthermore, gender is not accounted for, and research has shown that women tend to underperform men on the Motor and Visual scales (Vannieuwkirk and Galbraith 1985).

Split-half reliabilities are reported to range from 0.89 to 0.95, but as Lezak (2012) comments, "it seems logically improbable to perform split-half reliability studies on a test in which each item differs from its neighbour . . ." (p. 746). Internal consistency is generally in the 0.80 range (Golden et al. 1991).

Clinical Uses

Lezak (2012) summarizes the research on the clinical utility of the LNNB. The battery has shown a high level of accuracy in its ability to separate brain-injured from normal control subjects. It is also able to discriminate between chronic psychotic patients and those with neurologic disease, with hit rates of 73–74%. The LNNB does not fair as well when mild conditions are involved (a problem also noted on Christensen's original battery) and does not identify lesion laterality to a satisfactory degree. Research has demonstrated that the LNNB is not able to differentiate patients with focal lesions from those with diffuse damage. For example, research on patients with multiple sclerosis (MS; Stanley and Howe 1983) indicated that the patient group performed as well as normal controls on items that were supposed to reveal greater impairment, while the MS group did not perform significantly differently from brain-injured individuals on items on which better performance was expected. Aphasic patients were also studied (Ryan et al. 1988), and the LNNB was unable to discriminate between types of aphasic conditions.

Recent research has shown that the LNNB was able to detect motor changes in a group of Italian adolescents exposed to ferromanganese emission relative to nonexposed controls (Lucchinia et al. 2012), while Curral et al. (2012) found that LNNB deficits correlated with left frontal and temporal findings on magnetic resonance imaging in a case of a 55-year-old woman with multiple sclerosis and dementia.

A survey of battery choice in neuropsychological assessment (Retzlaff et al. 1992) indicated that only about 3% of neuropsychologists use the LNNB. This is due in part to the limitations noted above. Purisch (2001) wrote a paper in response to what he referred to as misconceptions about the psychometric properties and clinical utility of the LNNB. In his concluding remarks, Purisch wrote, “Application of the Lurian model to the data permits a deeper understanding of the primary neuropsychological functions that are of critical to formulating rational treatments, counselling and guidance, and analyzing components of behavioural functioning within the real-world context” (p. 279).

See Also

- [Boston Process Approach](#)
- [Halstead-Reitan Neuropsychological Test Battery](#)

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Luria, Alexander Romanovich (1902–1977)

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Major Appointments

- 1921–1923: Laboratory Assistant, Kazan Institute for the Scientific Organization of Labor, Kazan, Russia.
- 1923–1930: Staff Professor and Researcher, Institute of Psychology in Moscow, Moscow, Russia.

- 1930–1934: Head of Psychology department, Psychoneurological Institute at Kharkov University, Kharkov, Ukraine.
- 1934–1936: Research, Moscow Institute of Genetics; Department Head, Department of Clinical Psychology, Institute of Experimental Medicine, Moscow, Russia.
- 1939–1941: Head of the Laboratory of Experimental Psychology, Neurological Clinic of the Institute of Medicine (later called the Neurological Institute of the Academy of Medical Sciences), Moscow, Russia.
- 1941–1945: Commissioned to organize and run a hospital for soldiers during World War II, Cheliabensk, Russia.
- 1952–1958: Research Staff, Institute of Defectology, Moscow, Russia.
- 1945–1977: Professor of Psychology, Moscow State University, Moscow, Russia.
- 1945–1977: Head of Department of Neuropsychology, Moscow State University, Moscow, Russia.
- 1945–1950, 1958–1977: Burdenko Institute of Neurosurgery, Director of Neurosurgery Lab, Moscow, Russia.
- 1945–1977: Head of the Aphasiological Laboratory, Moscow Medical Institute, Moscow Russia.

Major Honors and Awards

- Ranked No. 69 on the list of top 100 psychologists of the twentieth century by *Review of General Psychology*.

Landmark Clinical, Scientific, and Professional Contributions

- The works of prominent psychiatrists such as Freud and Jung largely fueled Alexander Luria's initial interests in psychological theory. However, Luria was ultimately unsatisfied with the prevailing psychological theories of the time and set out to discover, "a psychology that would overcome [insufficiencies in knowing the complexity of people], that would simultaneously describe the concrete facts of

the mental life of individuals and generate general explanatory laws" (Cole, 23). In combination with friend and mentor, Lev Semionovitch Vygotsky, Luria ultimately studied psychological processes and cognitive abilities in diverse populations such as children with and without mental retardation and poorly educated rural women. They also performed some of the first studies investigating the role of genetics in cognitive functioning using monozygotic and dizygotic twins.

- After earning his medical degree, Luria began applying his knowledge of cognitive processes to those who had sustained neurological injury, work that was highly influenced by his care of World War II soldiers (see below). Luria's revolutionary theory of brain-behavior relations utilized many of the strengths of both localization and equipotentiality while also addressing many of their shortcomings. Luria posited the existence of three functional units within the brain, each responsible for a variety of functions necessary for both simple and complex behaviors (or cognitive abilities). The first functional unit encompasses the brain stem and diencephalon and is generally responsible for modulating arousal and filtering sensory input. The second functional unit utilizes cortical areas posterior to the central sulcus (i.e., the parietal, temporal, and occipital cortices) to perceive, integrate, and analyze sensory information. The frontal/prefrontal cortex comprises the third functional unit and is involved in a variety of cognitive abilities, generally termed executive functions, including planning, decision making, impulse control, and analyzing behaviors. The third unit can also modulate the level of cortical arousal (i.e., the first functional unit) through both direct and indirect processes.
- Luria believed that all behavior requires the brain to function as a whole but that each functional unit (or brain region) contributes in a unique way to a given behavior. Obviously, more complex behaviors require a larger functional network. Thus, the role of brain regions can be classified as pluripotential, given the limited or multifaceted contribution of each

region to behavior. An especially compelling aspect of Luria's theory is that it addresses recovery of function after injury. He believed that deficits caused by damage to one unit (or brain region) can, at least in part, be ameliorated by the spontaneous compensation of another area or through specific retraining. His idea of neural plasticity is profoundly insightful and has been supported through recent functional neuroimaging studies that have shown altered patterns of activation, following various forms of cognitive and physical rehabilitation.

- These and Luria's other contributions to the field of Neuropsychology are detailed in his works including *The Nature of Human Conflicts* (1932), *Higher Cortical Functions in Man* (1962/1966), *Restoration of Function After Brain Injury* (1963), *The Mind of a Mnemonist* (1968), *The Man With a Shattered World* (1972), *The Working Brain: An Introduction to Neuropsychology* (1973), *The Neuropsychology of Memory* (1976), and *The Making of Mind: A Personal Account of Soviet Psychology* (1979).

Short Biography

Alexander Romanovich Luria was born in Kazan, Russia, on July 16, 1902. His father was a gastroenterologist and his mother was a dentist. Luria moved to Moscow at the age of 15 when his father was appointed vice director of the Central Institute for Advanced Medical Studies. Luria excelled in school and used his knowledge of Latin as a springboard for learning English, French, and German. He earned a high school diploma in 1918 and entered Kazan University where he participated in many student-run discussion groups and became interested in man's role in society. Building on this interest in psychological processes, he read the works of Dilthey, Freud, and Jung. He also read, and translated into Russian, L. Brentano's *Theory of Human Drives*. These works were highly influential and increased Luria's desire to develop a more sound theory of psychological processes.

Luria graduated from Kazan University in 1921 and enrolled at both Kazan Psychiatric Hospital and the Pedagogical Institute to study medicine and psychology, respectively. In 1922, Luria formed a small psychoanalytic circle that he named the Kazan Psychoanalytic Association. One of the first things he did as head of the organization was send a letter to Freud, who gave Luria permission to translate one of his books into Russian. After further studying the available literature, Luria became critical of psychoanalysis and felt that it ignored the importance of social experience in cognition. In 1927, he resigned from the Psychoanalytic Society after his colleagues published harsh criticisms of Freud's work. Despite the fact that his own work conflicted with Freud, Luria refrained from denouncing Freud.

At the age of only 19, Luria accepted a position as a laboratory assistant at the Kazan Institute for the Scientific Organization of Labor. Later, he founded a journal called "Problems of the Psychophysiology of Labor and Reflexology." He later cited these events as significant in his development as a psychologist. Two years later, he secured his first staff appointment at the Moscow Institute of Psychology, where he and his colleagues studied emotional reactions in students preparing to take examinations, work that laid the foundation for an early model of the polygraph.

In 1924, Luria's career would forever change when he met Lev Semionovitch Vygotsky at the Second Psychoneurological Congress in Leningrad. Vygotsky was invited to join the staff at the Institute of Psychology, where Luria, Vygotsky, and Alexei Leontiev would essentially develop the field of cognitive psychology. In 1930, Luria and his colleagues founded a new Department of Psychology at the Psychoneurological Institute of Kharkov University. During the 1930s, the group began investigating the genetic basis and environmental influences on behavior (and cognitive functioning) by studying monozygotic and dizygotic twins. Using a series of cognitive tests, the group investigated the processes by which information is learned and remembered. Their results

suggested that individuals increased the use of various cognitive strategies with age and that both the genetics and the environment contributed to cognitive development.

Luria returned to medical school in 1936, and a year later, began a 2-year internship in neurology. After completing this training in 1939, he became head of the Laboratory of Experimental Psychology at the Neurological Clinic of the Institute of Medicine where he studied aphasia. In 1941, the Neurological Clinic in the Institute of Experimental Medicine commissioned him to organize a 400-bed hospital for soldiers injured during World War II. He had two major duties: (1) providing medical treatment for those who had sustained brain damage and diagnosing the effects of such injury and (2) developing a scientifically based rehabilitation program. During these experiences, Luria documented several types of aphasia and also implemented specific rehabilitation techniques using preserved abilities to compensate for damaged functions. His experiences during this time contributed significantly toward his theory of cortical functioning, which is described above.

In 1950, Luria was forced to leave his appointment at the Institute of Neurosurgery in Moscow when genetics was labeled a pseudoscience and banned from the Soviet Union. With the threat of arrest, he spent much of the next 8 years at the Institute of Defectology, also in Moscow, where he was essentially demoted and started as part of the research staff. After Stalin died in 1953, accusations against Luria were dropped and he eventually returned to the Institute of Neurosurgery in 1958 where he spent most of his remaining life, continuing to hold appointments at Moscow State University. During this time, he published two prominent case reports: the first documented a patient who seemed to have limitless memory (*The Mind of a Mnemonist*, 1968) and the second examined the cognitive deficits and gradual rehabilitation of a patient who sustained a bomb-induced lesion of the left parietal lobe (*The Man with a Shattered World*, 1972). One of Luria's most complete works was *Higher Cortical Functions*

in Man (1962), in which he presented a series of neuropsychological tests and discussed the process by which he determined cognitive deficits and lesion location.

Later in life, Luria followed a routine that involved writing in the morning and lab work in the afternoon and evenings with a nap in between. In 1977, his wife, Lana Pimenovna, was diagnosed with an inoperable tumor. Luria dedicated the rest of his time to caregiving and, for this reason, the couple moved to a sanatorium. He died of heart failure while on the telephone trying to obtain a new medication for his wife. She lived another 5 months and, during this time, was able to archive and organize Luria's memorial office at Moscow State University, where she also donated his personal library. He profoundly influenced many prominent neuropsychologists including Anna-Lise Christensen and Elkhonon Goldberg, who played a large role in introducing Luria to the West.

Cross-References

- [Equipotentiality](#)
- [Christensen, Anne-Lise \(1926–\)](#)

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Luxury Perfusion

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Definition

Luxury perfusion is a term originally used to describe the dilation of numerous vascular channels observed within the relatively avascular infarcted area of the brain 24–48 h after an ischemic stroke. At surgery, the infarcted area thus appears to contain an increase in the number of blood vessels. These are not actually functioning to supply the infarcted brain, however, so do not represent true “perfusion.”

On a contrasted CT scan, this phenomenon is perceived as an area of enhancement (increased density or whiteness) at the margin of the infarct. This is visible 1 day to several days after a stroke.

With the development of metabolic studies and PET scanning, the term was equated with low oxygen extraction ratio. SPECT scanning suggests that spontaneous reperfusion after cerebral infarction occurs often but is rarely associated with clinical improvement.

Luxury perfusion has been shown via SPECT in cases of successful thrombolysis after ischemic cerebrovascular accident.

The term luxury perfusion may also refer to a hyperperfusion syndrome occurring in 0.2% of patients undergoing cerebral endarterectomy. This condition is characterized by ipsilateral headaches, hypertension, seizures, and focal neurologic deficits. The mechanism of “luxury perfusion syndrome” is a severe impairment of cerebral autoregulation and postoperative hypertension, with increased cerebral blood flow to a previously hypoperfused hemisphere. The associated intractable headache usually improves with upright posture. Transcranial Doppler study may demonstrate abrupt increase flow velocities in the middle cerebral artery, and diffuse hyperintensity may be demonstrated transiently on diffusion-weighted MRI in

the distribution of the involved arterial territory. This syndrome, if not recognized and treated appropriately, may lead to the development of cerebral edema, with severe morbidity or death.

Cross-References

► [Carotid Endarterectomy](#)

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Lyme Disease

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Synonyms

Borreliosis

Short Description or Definition

Lyme disease, caused primarily by *Borrelia burgdorferi* sensu stricto in the USA, and by the

closely related spirochetes *B. afzelii* and *B. garinii* in Europe, is transmitted by hard-shelled Ixodes ticks. Typically, 3–30 days after the tick bite, there is a slowly expanding flat rash, known as erythema migrans (EM) which often has a central clear area giving it a “bull’s-eye” appearance. In children this rash occurs in up to 90% of infected individuals (Pediatric Lyme Disease Study Group et al. 1996); in others it either does not occur or goes unnoticed. The infection can disseminate, causing multisystem involvement. The Lyme disease case definition (Centers for Disease Control and Prevention 1997) is a person with EM or with at least one characteristic late manifestation and laboratory confirmation of the infection.

Categorization of Systemic and Neurological Involvement

Infection may be accompanied by fatigue and malaise. Disseminated disease may involve the skin (multifocal EM, or with European strains, acrodermatitis atrophicans), joints (recurrent episodes of primarily larger joint arthritis), heart (conduction abnormalities), liver, or nervous system. Neurologic Lyme disease, referred to as neuroborreliosis, was first reported in 1922 (Garin and Bujadoux 1922). Common manifestations include lymphocytic meningitis, facial (or other cranial) nerve palsy, and radiculoneuropathy. Encephalitis, encephalopathy, and neuropsychological impairments have been a particular focus of investigation (Halperin et al. 1989; Kalina et al. 2005; Kaplan et al. 1992; Krupp et al. 1991; Logigian et al. 1990). Encephalopathy, abnormal cognitive functioning without apparent underlying structural brain involvement, typically improves after antibiotic therapy (Halperin et al. 1989; Logigian et al. 1990). Some studies have suggested that cognitive deficits might persist in some individuals for variable durations after usually effective antimicrobial treatment (Benke et al. 1995; Bujak et al. 1996; Fallon et al. 2008; Krupp et al. 1991). Recent prospective studies (Ogrinc et al. 2016; Wormser et al. 2015a) suggest that if such a disorder exists, its long-term impact on

quality of life is usually minimal. Importantly, recent studies (Dersch et al. 2015, 2016) suggest these symptoms are not related to nervous system infection, past or ongoing.

Epidemiology

Lyme disease is the most common tick-borne illness in Europe and the USA. There has been a slow, steady increase in the number of cases meeting the CDC case definition (now about 30,000/year), as the geographic footprint of this zoonosis has gradually expanded. Notably, a recent estimate extrapolated from laboratory testing suggests there might be as many as ten times that number of patients diagnosed with and treated for Lyme disease annually (Hinckley et al. 2014).

Natural History

Following antibiotic therapy, the vast majority of patients fully recover; rare instances of persisting infection typically resolve with an additional course of antibiotics, often parenteral. Some patients experience an ongoing relapsing arthritis, thought to be immune mediated. Individuals with neuroborreliosis may have residua related to structural damage to peripheral or cranial nerves or rarely the parenchymal central nervous system—damage that may resolve slowly or not at all.

Some patients describe persisting symptoms following usually curative antimicrobial treatment—most commonly fatigue, musculoskeletal pain, and memory problems (Cairns and Godwin 2005)—symptoms that overlap with those of chronic fatigue syndrome (CFS) (Gaudino et al. 1997). The etiology of these symptoms remains unclear. There is no microbiologic evidence that such individuals have persisting infection and symptoms do not improve in any consistent or persistent fashion following antimicrobial therapy (Berende et al. 2016; Fallon et al. 2008; Klempner et al. 2001; Krupp et al. 2003). Whether this is a distinct nosologic entity, anchoring bias in individuals who relate nonspecific

symptoms to previously diagnosed Lyme disease or an example of a more general phenomenon that may affect some individuals after the stress of a medical illness remains to be established.

Neuropsychological Findings in Lyme Disease and Those with Persisting Symptoms After Antimicrobial Therapy

Memory and other cognitive deficits have been documented in untreated and treated Lyme disease patients with cognitive symptoms. In one study, untreated patients with Lyme disease and neurocognitive symptoms were compared to others with fibromyalgia or depression. About 14 of the 27 patients tested had impairments on either the Wechsler Memory Scale (WMS), California Verbal Learning Test (CVLT), or Rey Osterrieth Figure Test (Kaplan et al. 1992; Logigian et al. 1990). Among 15 such patients evaluated a mean of 6.7 months after completing antibiotic therapy, deficits relative to healthy controls were noted on all the subtests of the Selective Reminding Test with the exception of recognition and recall. Deficits were also present on the WMS-revised (WMS-R) and the Controlled Oral Word Association Test (COWAT) (Krupp et al. 1991). The cognitive differences between patients and healthy controls remained significant even after controlling for differences in depressed mood (Krupp et al. 1991). Other impairments in these individuals include poor performance on attention and verbal memory tests from the WMS-R (Bujak et al. 1996), poor mental flexibility, impaired verbal fluency, and slowed cognitive processing speed (Benke et al. 1995; Pollina et al. 1999). Some studies suggest that persisting symptoms relate to underlying resilience (Hassett et al. 2010).

Children with untreated Lyme disease may also have neurocognitive difficulties during infection, consisting of mild-to-moderate deficits on auditory and visual sequential processing (Bloom et al. 1998). In contrast to adults, though, among 41 pediatric posttreatment cases, no differences in cognitive functioning were identified, compared to controls (Adams et al. 1994).

Evaluation

The assessment of Lyme disease requires a careful history and physical examination. Antibody testing in the blood or CSF consists of IgM and IgG ELISA and IgM and IgG Western blot. However, within the first 2–4 weeks of the infection, these tests can be negative. A complete blood cell count and electrolytes will screen for abnormalities associated with coinfection from other agents.

While nervous system magnetic resonance imaging (MRI) may demonstrate focal areas of inflammation in rare instances of CNS parenchymal involvement (Hattingen et al. 2004; Kalina et al. 2005), the significance of older, uncontrolled reports of nonspecific small areas of non-enhancing increased signal (Fernandez et al. 1990) is questionable. While quantitative cerebral blood flow studies in groups of patients with long-standing infection have demonstrated cerebral white matter hypoperfusion (Fallon et al. 2008; Logigian et al. 1990), these findings are nonspecific (Logigian et al. 1990). Neuropsychological testing may be informative in patients with symptoms of memory or cognitive problems.

Treatment of Localized, Disseminated, and Persistent Symptoms After Treatment for Lyme Disease

Antibiotic treatment is the mainstay of therapy. For localized infection, oral treatment is sufficient, in adults usually with doxycycline 100 mg twice a day for 10 days. With disseminated infection, with manifestations such as facial palsy, cardiac conduction block, or arthritis, oral therapy should be given for longer periods (21–30 days). IV ceftriaxone is usually reserved for patients who have failed oral therapy or who have demonstrable parenchymal CNS involvement.

Management of Persistent Symptoms After Antimicrobial Therapy for Lyme Disease

How to manage patients with persisting symptoms after antimicrobial treatment for Lyme disease has been the subject of much debate; varying opinions can be found in the literature (Hurley and

Taber 2008). Clinical guidelines (Halperin et al. 2007; Wormser et al. 2006), based on high level studies (Berende et al. 2016; Fallon et al. 2008; Klempner et al. 2001; Krupp et al. 2003), conclude that repeated or prolonged courses of antibiotic therapy are not effective. The reported impact of these symptoms on quality of life (QOL) varies among studies. Longitudinal prospective studies of patients with acute Lyme disease (Wormser et al. 2015a, b) suggest that the impact is only substantial when attributable to other etiologies. Treatment trials in which patients were selected for highly impactful symptoms did not surprisingly find such individuals to have greatly diminished QOL.

Importantly, in at least one such trial, no cognitive impairments were identified at baseline in these patients (Kaplan et al. 2003). In another, in which subjects with persistent and severe fatigue were randomized to receive 1 month of IV ceftriaxone or of IV placebo (Krupp et al. 2003), the ceftriaxone-treated group showed improved fatigue scores (but not cognitive) compared to the placebo group at the end of treatment, a difference that disappeared at 6 months of follow-up.

A similar study (Fallon et al. 2008) examining the response of cognitive deficits in this population to additional antibiotics came to different conclusions. In this study, focusing exclusively on patients with documented cognitive impairment after appropriately diagnosed and treated Lyme disease, individuals were randomized to receive either IV ceftriaxone or IV placebo for 10 weeks. A treatment benefit on memory performance was observed at week 12, but this benefit was not sustained at 24 weeks. Unlike the other study (Krupp et al. 2003), treatment had no effect on fatigue scores. Further, adverse events were associated with IV therapy. Taken together, these clinical trials do not support treating patients with persisting symptoms with additional antibiotics (Fallon et al. 2008; Kaplan et al. 2003; Klempner et al. 2001; Krupp et al. 2003). On the other hand, symptomatic therapies for pain or depression should be considered.

In summary, most patients with Lyme disease respond well to antibiotic therapy. During active infection, some patients experience cognitive impairments; these usually improve following

therapy. Following appropriate antimicrobial therapy, a subgroup of patients may have persisting cognitive symptoms, fatigue, pain, and reduced quality of life. These problems do not respond to additional antibiotic treatment, and their relationship to antecedent Lyme disease is unclear. Alternative therapeutic approaches for persistent symptoms need to be developed.

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Lymphoplasmacytic Tumor

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Synonyms

Lymphoplasmacyte-rich tumor

Definition

Lymphoplasmacytic tumors are composed of lymphocytes and plasma cells. Within the CNS, lymphoplasmacytic tumor presents as a lymphoplasmacyte-rich meningioma (LRM) (previously designated inflammatory meningioma). Being an extremely rare variant of meningioma, LRM demonstrates inconsistent biological behavior and clinical course. The LRM is composed primarily of inflammatory cells and subsequently presents as clinically similar to hematological abnormalities rather than typical meningiomas (Yamaki et al. 1997). Mean age of onset is 34 years of age. LMRs are unresponsive to anti-inflammatory therapy and are primarily treated by means of surgical debulking, when feasible. Radiotherapy is not recommended, and hormonal or immune-inhibitor therapy is being

explored as a possible secondary treatment (Zhu et al. 2013).

Cross-References

► [Meningioma](#)

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